ABSTRACT

Title of dissertation: NEURAL CONTROL OF SPEED IN HUMAN WALKING

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The central nervous system in humans continuously controls the speed of walking by modulating muscle activities. The underlying mechanisms of this control process are not well understood. Recent studies have probed the neural control of walking using sensory and mechanical perturbations. It has been suggested that transient responses to perturbations show patterns in the modulation of muscle activations not previously observed. This dissertation aims to systematically investigate differences in modulations of muscle activations between transient responses and steady-state walking. Three studies were designed to explore these modulations using visual and mechanical perturbations. The first study compared the qualitative patterns from transient responses to visual perturbations to those observed during steady-state walking. Small changes in the average muscle activations between two steady-state speeds were compared to small transient changes due to perturbations. We demonstrated that the decrease in the plantarflexor activity during transient responses that potentially contributed to an increase in speed was unique to these

responses and not reproducible in steady-state walking conditions. The second study quantified the effects of average walking speed on transient responses to visual perturbations and compared these effects to steady-state walking conditions. A scaling effect on the amplitude of responses was shown across different treadmill speeds. Finally, in the last study, we explored characteristics of transient responses to mechanical perturbations of the treadmill. We examined the effects of perturbations at two different amplitudes on both kinematics and muscle activations. The responses of the neurofeedback to kinematic deviations were quantified and it was shown that the local limit cycle approximation was reasonable to describe the system. Together these studies shed light on how modulations of muscle activity are utilized by the nervous system to regulate the key variable of walking speed, as well as other aspects of human locomotion.

NEURAL CONTROL OF SPEED IN HUMAN WALKING

by

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for mom and dad who didn't make it

for all the love I couldn't give them

&

for Farzaneh who will

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List of Abbreviations

sec	second
msec	millisecond
Hz	hertz
m	meter
deg	degree
mV	millivolt
Ipsi	Ipsilateral
Contra	Contralateral
AP	Anteroposterior
ML	Mediolateral
EMG	Electromyography or electromyogram
TA	Tibialis anterior
SOL	Soleus
GAS	Gastrocnemius
GASl	Gastrocnemius lateralis
GASm	Gastrocnemius medialis
RF	Rectus femoris
VASl	Vastus lateralis
VASm	Vastus medialis
BF	Bicep femoris
SEMT	Semitendinosus
TFL	Tensor fasciae latae
GLmax	Gluteus maximus
GLmed	Gluteus medius
ESL	Erector spinae lumbar
EST	Erector spinae thoracic
iX	ipsilateral X (e.g. iSOL means ipsilateral soleus)
cX	contralateral X
TN	Tibial nerve
PTN	Posterior tibial nerve
MpN	Medial plantar nerve
SuN	Sural nerve
TMS	Transcranial magnetic stimulation
IR	Impulse response
SR	Step response

IRF	Impulse response function
φIRF	phi-IRF (phase dependent IRF)
FRF	Frequency response function
TF	Transfer function
HTF	Harmonic transfer function
LTI	Linear time invariant
LTP	Linear time periodic
LLC	Local limit cycle

1

Introduction

> Whenever a theory appears to you as the only possible one, take this as a sign that you have neither understood the theory nor the problem which it was intended to solve.
>
> Karl Popper, philosopher of science

1.1 Why study walking

Mobility impairment has a significant impact on the health of the elderly population. Between 2008 and 2012 more than ten million adults in the US aged 65 and older reported having difficulties in walking or climbing stairs [1]. Another population affected by movement disorders is patients with pathological gait. Parkinson's, cerebral palsy, sclerosis and stroke are among many neurological disorders that result in walking abnormalities. The Parkinson's Disease Foundation reports that about 60,000 Americans are diagnosed with the disease each year and the total costs of it amounts to $25 billion per year [2]. Fall related injuries in people 65 and older has been another consequence of mobility impairment. Costs of treating fall injuries to Medicare surpassed $31 billion in 2015 [3]. These statistics emphasize the urgency of addressing walking-related health care issues by the scientific community. A comprehensive understanding of the mechanisms involved in the control of gait may assist researchers in developing more effective diagnostic and therapeutic procedures for rehabilitation.

1.2 The problem to be solved

Control of gait requires control of speed, which is a fundamental parameter in the assessment of gait characteristics [4]. Previous studies have shown that declines in speed of gait are correlated with health decline in neurological and geriatric populations [5–7]. However, it is not clear if the change in speed is the cause of

health issues or merely a concurrent event observed during ambulatory difficulties. Further research is required to better understand how walking speed is altered in different populations. Control of walking speed is a task performed by the central nervous system (CNS) in a continuous fashion in the face of perturbations from the environment and internal noise. Studying the responses to small sensory or mechanical perturbations of walking can shed light on the underlying mechanisms used by the CNS to control speed. The goal of this research is to focus on this problem through a series of studies that probe the neural control of walking using visual and mechanical perturbations.

1.3 How to solve it

To understand how the CNS controls the walking speed, it is necessary to investigate the causal relationship between changes in the control signals from CNS (i.e., muscle activations) and changes in speed. To elicit transient changes in the activity of muscles and the speed of walking, we can apply pseudo-random perturbations to walking trials. The cause and effect relationship between the perturbation as the input to the biological system and the response of the system as the output can be identified using system identification techniques. System identification is a branch of systems theory that characterizes behavior of a system through its interactions with the environment [8]. The relationship between the input and the output of a system can be quantitatively described in the form of a mathematical model. This description could take the form of a parametric model, typically a

system of differential equations with parameters, or a non-parametric model such as a frequency response function (see below). While the non-parametric approach may require a larger number of measurements to obtain an accurate description of the system, the parametric approach often requires an in depth knowledge of the system and uses more assumptions in modeling. Because of this, parametric system identification may result in unreliable prediction for complex systems where our understanding of the system is insufficient. Non-parametric system identification has been successfully applied to study of human movement in the past. Ankle dynamics [9, 10], control of arm posture [11, 12], head and neck movements [13, 14] and balance control [15–18] have been among some applications of system identification to reveal the underlying mechanisms of movement control in humans. Here we use a non-parametric approach as control of walking in humans is a complex task involving many degrees of freedom.

Recently the use of system identification techniques has been expanded to study of human locomotion as a rhythmic behavior [19] and using an analysis technique that can potentially reveal the control mechanisms of walking. Figure 1 depicts a schematic of the neural control process involved in walking. The motor command, u(t), measured with electromyography (EMG) is sent to the plant (i.e., muscles and skeleton) which results in movement, y(t), measured as kinematics with a motion capture system. The movement is encoded by sensory systems (i.e., vestibular, somatosensory and vision) and sent to the neural controller. At different parts of the loop, perturbations could be applied and responses could be measured to identify properties of the plant (P) or the neurofeedback (F).

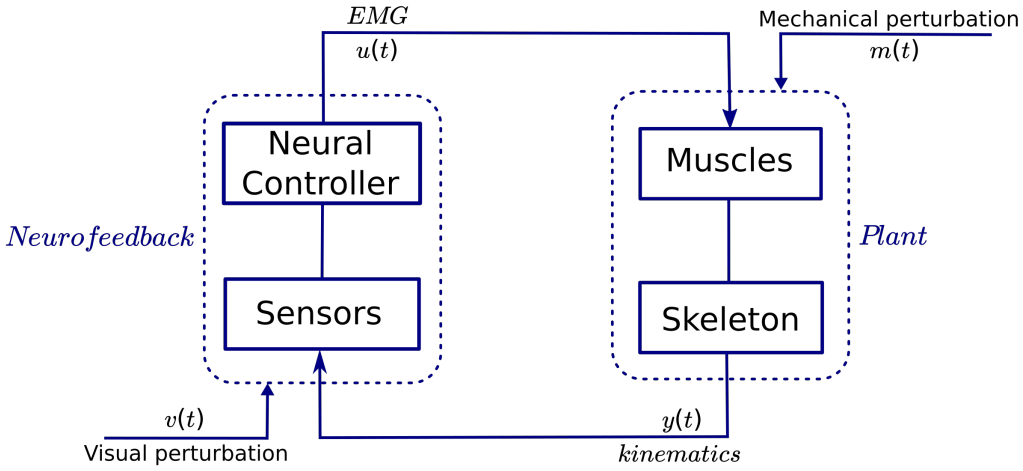

Figure 1.1. Block diagram of neural control of walking. On the right the plant maps the control signals (u(t)) to kinematics (y(t)) and on the left neurofeedback maps kinematics to control signals.

For linear time invariant (LTI) systems, properties of any part of the loop can be expressed with its frequency response functions (FRFs). The gain function of FRFs is the ratio of the input amplitude to the output amplitude and the phase function describes the temporal shift (relative to the cycle period) between the input and the output. If a mechanical perturbation, m(t), is applied to the system, then $T_{mu}(f) = F(f)T_{my}(f)$ (where T_{ab} denotes the FRF from input a to output b), allowing us to identify some of the properties of neurofeedback F(f). With a sufficient number of different mechanical perturbations, it may be possible to fully identify F(f) [18]. Similarly, if a visual perturbation, v(t), is applied to the system, then $T_{vy}(f) = P(f)T_{vu}(f)$, allowing us to identify some of the properties of plant P(f). These relationships describe the method of joint input-output (JIO) system identification which provides estimates for the plant and the controller without the need for any prior knowledge of these blocks [20, 21]. Without the use of JIO

method, we can still infer properties of the system by looking at the EMG responses (i.e., output of the neurofeedback) when applying visual perturbations. However, this method of inference requires us to make assumptions about the function of the neural controller. For instance, when during visual perturbations the visual scene moves away from the subject, we assume this creates the illusion of being left behind and the response of the nervous system (i.e., neural controller) to this stimulus is to increase muscle activity in order to increase the speed. This method of inference is called short-latency inference [19]. Both JIO and short-latency inference are useful in understanding the underlying mechanisms of locomotion in humans.

1.4 Organization

Chapter 2 provides a review of the literature. The relationship between speed and muscle activity has been investigated mostly by modulating speed and observing its effects on muscle activations. We summarize the key findings of studies in this area. To investigate the effect of changes in muscle activations on modulation of speed we apply small perturbations to walking. The available knowledge from the effect of visual perturbations on walking behavior will be discussed first. Then we present the effects of mechanical perturbations on walking explored by previous studies. We discuss the findings from studies that applied joint perturbations as well as surface perturbations.

Chapter 3 compares the qualitative patterns from transient responses to visual perturbations to those observed during steady-state walking. Across all phases of the

gait cycle small changes in the average activity between two steady-state speeds will be compared to small transient changes due to perturbations. The effect of transient changes in muscle activity on transient changes in speed will be investigated as well. Additionally, the mean waveforms of activity between steady-state walking and transient responses will be compared.

Chapter 4 quantifies the effects of average walking speed on transient responses to visual perturbations and compares these effects to steady-state walking conditions. Transient responses will be measured at three substantially different treadmill speeds and they will be compared to changes in mean waveforms of unperturbed walking across different speeds.

Chapter 5 explores characteristics of transient responses to mechanical perturbations of the treadmill. We examine the effects of perturbations at two different amplitudes on both kinematics and muscle activation responses and compare the results between ipsilateral and contralateral legs. The responses will be separately discussed for single-support and double-support phases.

2

Literature review

All that stuff is tried! With a new problem, where we are stuck, we are stuck because all those methods don't work! If any of these methods would have worked, we would have gone through there.

Richard P. Feynman

Nobel laureate in Physics 1965

2.1 Muscle activity and speed of walking

Changes in muscle activity can result in changes in the speed of walking. This is how humans naturally control their speed. However, changes that affect the speed of walking (e.g. slipping on ice) can result in people changing their muscle activity in order to regulate their speed. So the relationship between muscle activity and speed is bidirectional. Some effects of changes in speed on muscle activity have been explored in the past. The current knowledge available from the literature on walking at different speeds assumes a direct relationship between the level of activity of lower extremities muscles and speed. Several studies in the past have looked into this relationship for walking under steady-state conditions. In this section, we review these studies and their findings.

Hof et al. [22] were one of the first groups to measure surface electromyograms (EMG) from subjects walking at different speeds. EMG was measured for ten walking steps at five speeds (range: 0.75–1.75 m/s). Close to the peak of activity, EMG profiles showed considerable changes with speed while away from the peak changes were small. The authors suggested that the activity at any speed could be estimated through a linear interpolation of the sum of the profile at the lowest speed and a function that represents the increase in the activity per unit increase of normalized speed. Because of lack of statistical tests, conclusions made about the effect of speed on the muscle activity may not be reliable over the entire gait cycle since it is not clear whether small changes in the activity away from the peak were statistically significant or not.

den Otter et al. [23] expanded the previous work by testing the changes in muscle activations as a function of speed for a wider range (0.06–1.39 m/s), including very low speeds. It was shown that a reduction in the speed of walking in most of the lower extremities muscles results in lower activations. An interesting finding of this study was the exceptions to this rule. In biceps femoris (BF) at lower speeds, an increase in the activity was observed during late stance. For very slow speeds rectus femoris (RF) activity during the late swing showed an inverse relationship with speed. Another finding was the lack of a relationship between the activity of tibialis anterior (TA) and speed during early swing, a part of the gait cycle in which the function of foot clearance is mainly attributed to TA activity. The authors also did not observe any speed dependent component in the activity of calf muscles during early to mid-stance. Similar to Hof et al. [22], this study did not include any statistical analysis.

Another foundational study by Neptune et al. [24] that looked into the speed versus EMG modulation was a modeling study that inferred the functional role of each muscle through the application of forward dynamics simulations. The authors showed that their model reproduced the general patterns of activity observed in experimental studies discussed. The muscle works of soleus (SOL) and gastrocnemius (GAS) were almost constant in mid stance, but they increased significantly with speed in late stance. Increases in the activities of SOL and RF with speed resulted in more propulsion for the trunk. Hamstring showed an increase in the activity at higher speeds, which contributed to the deceleration of the leg during late swing.

In addition to the key studies reviewed above, several others have measured

changes in activation profiles as a function of speed as part of their experiment designs [25–28]. These studies have used modeling and experimental approaches to understand the contribution of each muscle to modulation of different kinematic or kinetic parameters of gait at different phases of the cycle. Other studies [29–32] have focused on the changes in the activity of a particular muscle in healthy subjects as the speed changes or activity of groups of muscles in patient populations in order to better identify the role of muscles in control of speed for rehabilitation purposes. An important characteristic shared by all of these studies is the fact that they all have measured changes in muscle activities at different speeds for steady-state walking.

While the study of muscle activations at steady-state conditions provides an idea of general patterns of activity at different speeds, the assumption of steady-state is far from the way humans normally walk. Acceleration and deceleration, obstacle negotiation, disturbance rejection and turning are all examples of behavior that require modulation of walking speed which is in turn driven by transient changes in muscle activations. A few studies in recent years have explored characteristics of transient walking [33–35]. It has been suggested that control of speed works through modulation of braking and propulsive impulses and to increase speed subjects change the braking impulse more than the propulsive one [34]. Such a finding about control strategies involved in walking and their implementations by the nervous system through modulation of muscle activations could only be achieved by looking at walking behavior under transient conditions.

2.2 Visual perturbations of walking

Different spinal and supraspinal pathways contribute to neural control of walking under perturbations. These pathways and their role in control of gait have been extensively studied in the literature [36–38]. In this section we review the application of visual perturbations to probe neural control of walking. We limit our review here to a perspective that is focused on the system as a black box and does not elaborate on specific neural circuits involved in control of walking.

A systematic analysis of the role vision plays in locomotion was first presented by Gibson [39]. He highlighted major unanswered questions in this area such as how animals use visual information to avoid a collision or how they achieve the perception of their speed relative to other objects in the environment. He argued that the reason for a lack of advancement in answering these questions at the time was the belief that the response to light was physiological while the response to objects was psychological. He proposed a unified theory of visual control of locomotion to fill this gap. While Gibson's effort was useful in organizing and defining the important concepts, his work and some other early studies (e.g., [40]) in the area of visually guided locomotion was mainly focused on the ecological aspects of the motor task. In the remainder of this section we will limit our review to studies which focused on the effects of optic flow on motor control mechanisms involved in locomotion.

One of the first studies to manipulate the velocity of the optic flow to quantify its effects on gait parameters such as stride length and cadence was performed by Pailhous et al. [41]. To control the visual scene, a pattern of luminous spots was pro-

jected on the floor around the subjects. The visual pattern was then moved forward or backward when subjects were walking in the room. Both forward and backward movements of the visual scene resulted in significant decreases in stride length with the effect of backward movement being more prominent. The cadence was increased during forward flow while the backward flow decreased it. The importance of these results lies in the finding that manipulation of visual information in both directions leads to responses from subjects even though the information from other sensory systems is still intact and accurate.

Naturally humans rarely walk in a straight line. To better understand the role of vision in control of locomotion in natural environments, Patla et al. [42] designed a series of experiments that investigated direction control and obstacle avoidance in walking. They used sudden changes in visual cues to instruct subjects to modify their walking path. Their results showed that humans cannot change their direction of movement during an ongoing step and direction control had to be preplanned. This inability in changing directions instantly was attributed to the lack of powerful ankle invertors-evertors in humans. Unlike direction control, subjects showed the ability to modify their gait during a step in response to changes in obstacle height and location. Patla et al. proposed that a combination of different strategies such as a change in elevation of the foot during the swing or lifting of the swing leg through increasing the stance push-off might explain the successful responses to perturbations.

Konczak [43] examined the extent to which the location of stimulus in the visual field influences control of locomotion and found that changes in the optic flow

affects the step velocity. He designed an experiment to compare kinematic changes in gait due to perturbations in the central versus peripheral field of view. The subjects walked in a room with eyes open or closed. The entire room including the floor was moved during some trials to manipulate subjects' perception of speed. Other trials used movements of side walls or the front wall to create peripheral versus central disturbances. It was observed that all conditions compared to the normal vision resulted in significant changes in the mean step velocity. The backward flow led to a decrease in step velocity while the forward flow induced an increase. Konczak argued that the slow down and the speed up effects were the results of subjects trying to match their speed to the speed of optic flow. The peripheral stimulation resulted in similar effects compared to the central one.

To understand how control of locomotion relies on the interaction between the visual feedback and other sensory modalities, Prokop et al. [44] designed an experiment to explore the roles of vision and proprioception in control of walking speed in a closed loop setup. They measured the position of the subject on a self-driven treadmill and used this to design a feedback loop to keep the treadmill speed close to the desired speed of the subject. The optic flow relative to subject's walking speed was changed to mimick slower or faster speeds. The results showed an inverse linear relationship between changes in the relative optic flow and the changes in speed and step length while no changes were observed in the step frequency. Based on this finding the authors suggested that visual information modulated the spatial component (i.e., step length) of leg movement while proprioceptive input modulated the temporal component (i.e., step frequency). When the relative optic

flow increased, the perception of speed that comes from visual input created the illusion that subjects were moving faster than their real speed which was reported through proprioception. As a result, subjects slowed down and hence the inverse relationship between relative optic flow and walking speed.

Although many studies manipulated the optic flow to understand responses to visual perturbations, the idea that this manipulation was the cause of subjects modifying their locomotor behavior was mainly based on the work of Gibson [39,45] which suggested humans kept the focus of the optic flow on the target they wanted to navigate to. Since the optic flow and the navigation path are naturally aligned it is not possible to know whether people actively align these two as part of their navigation strategy. Taking advantage of virtual reality technologies, Warren et al. [46] investigated this question for the first time by creating a mismatch between the direction of movement and the direction of the optic flow. The goal was to find out if humans used the optic flow to steer their locomotion (Gibson's assumption) or an ego centric direction strategy which is aligning the body to the target was used as suggested by some studies [47–49] or the real strategy in use was a mix of these two. To implement this idea, subjects were asked to wear a stereoscopic head-mounted display while walking towards a target. The center of the optic flow was dislocated towards the right or left by 10° in each trial. If subjects navigated based on the optic flow their path should have been a straight line. However, if ego centric direction was used for navigation subjects must have been constantly reorienting towards the object to minimize the mismatch between the optic flow and the target. This would have resulted in a curved path. Warren et al. showed that in absence

of any optic flow people used ego centric direction to steer their locomotion while greater optic flow influenced locomotion more. This validated Gibson's assumption and further expanded our knowledge that ego centric direction also played a role in steering locomotion.

That humans reorient themselves upon changes in the optic flow has been established through elaborate research. However, it was not clear whether this behavior was dependent on the speed of locomotion. Jahn et al. [50] investigated this by applying perturbations to the optic flow in the roll plane for walking and running at different speeds. Subjects wore prism goggles that tilted their optic flow 15° from vertical while instructed to walk or run in a straight line. Drifts towards the direction of the tilt were observed in most subjects. The increase in speed of locomotion significantly increased the amplitude of deviations. It was concluded that similar to the effects of vestibular input [51, 52], perturbations of the visual input had greater effects on control of locomotion at lower speeds. A possible explanation of this effect was the involvement of highly automated spinal locomotor programs at higher speeds. A similar reduction of responses were observed for proprioceptive input with increases in speed [53, 54].

In addition to the impact of locomotion speed on effects of changes in the optic flow, how fast the optic flow is modulated can also affect gait parameters. Mohler et al. [55] tested the effect of optic flow speed on preferred walking speed and the walk-to-run and run-to-walk transition speeds. Subjects walked on a treadmill in a virtual reality room at their normal pace as well as walk-to-run and run-to-walk transition trials. During trials, the visual scene was moved faster, slower or at the same speed as

the subject. Faster optic flow reduced both walk-to-run and run-to-walk transition speeds while slower optic flow had an opposite effect. In the second experiment, subject chose their comfortable speed of walking under optic flows faster, slower or moving at the same speed as the subject. The preferred speeds were 1.41, 1.29 and 1.21 m/s for slow, normal and fast optic flows respectively. The effect of visual speed on preferred speed was statistically significant. Although a relationship was found between the speed of the optic flow and the gait speed this relationship was not linear. When the speed of visual scene was increased by two folds, the preferred and transition speeds were changed by less than 10%.

While many studies showed different aspects of the relationship between the optic flow and the speed of walking, it still remained a question which properties in the optic flow affected the perception of speed during locomotion. François et al. [56] proposed that two specific properties named the global optic flow rate (GOFR) and the edge rate (ER) were used by humans in the estimation of self-motion velocity. GOFR is the angular velocity of texture elements in a direction and ER is the number of texture elements per unit of time passed in that same direction [57]. GOFR can be modulated by eye height. For instance, increasing the eye height (i.e., showing the visual scene from the point of view of a taller individual) gives people the illusion they are walking slower than their actual speed. Changing the texture density can affect ER. Increasing the texture density (i.e., more objects passing the view at each gait cycle) results in the perception of walking faster. François et al. asked subjects to walk on a treadmill in a virtual reality room while GOFR and ER were modified by a factor of 0.5 or 2 at a time. The results showed that compared to the changes in

the texture density, changes in the eye height elicited larger speed modifications in subjects. Participants achieved these modulations using a combination of changes in the step length and the step duration. This study showed that humans can modify their preferred speed by 16% to meet the optical constraints during walking.

Many studies have shown modulations of walking in response to changes in the optic flow. However, the control of step by step changes in gait parameters during perturbations has not received enough attention. A key question here is whether humans control the speed, stride length and stride duration of their walk under visual perturbation within each stride. A recent study by Salinas et al. [58] targeted this question using five visual conditions in a virtual reality setup. Subjects were asked to walk on the treadmill looking at a 180° semi-cylindrical screen in front of them. The testing conditions were no visual scene (i.e., blank screen), a static scene, a scene moving slower than subject's speed, a scene moving faster and a scene matched to the speed of walking. It was found out that in static scene condition subjects corrected the stride speed fluctuations more rapidly compared to other conditions. Also, the variability in the stride speed was less in this condition compared to non-zero optic flow conditions. During no visual scene, participants showed a more cautious way of walking with their steps becoming shorter and their step rate to increase. These results show how the temporal features of the optic flow is used to correct deviations from the desired speed on a stride to stride basis.

2.3 Mechanical perturbations of walking

Unlike visual perturbations that presumably affect walking speed by changing the perception of motion, mechanical perturbations directly change the speed of limbs. Also unlike visual perturbations which contribute to modulation of speed through supraspinal input, mechanical perturbations can result in both spinal and supraspinal reflexes. In this section, we give a detailed review of effects of mechanical perturbations on neural control of movement. Before looking into the findings of the most frequently cited studies in the field, it helps to highlight some of the major physiological elements involved in the sensorimotor control of responses to mechanical perturbations. Figure 2.1a shows the neural connections at the muscle level. Changes in length and velocity upon perturbation are detected by muscle spindles (types Ia and II afferents) and changes in forces are sensed by Golgi tendon organs (GTOs). These afferent sensory signals are sent to the spinal cord (Figure 2.1b) or the brain. In case of a spinal reflex, the afferent input can initiate a response through monosynaptic (e.g., stretch reflex) or polysynaptic connections (e.g., withdrawal reflex from pain receptors) which results in the motor commands from α or γ motoneurons being sent to the extrafusal or intrafusal muscle fibers through efferent pathways. A more detailed explanation of all the elements involved in anatomy and physiology of reflexes is beyond the scope of this dissertation. The enthusiastic reader is advised to consult neurophysiology books (e.g., [59]) for further information.

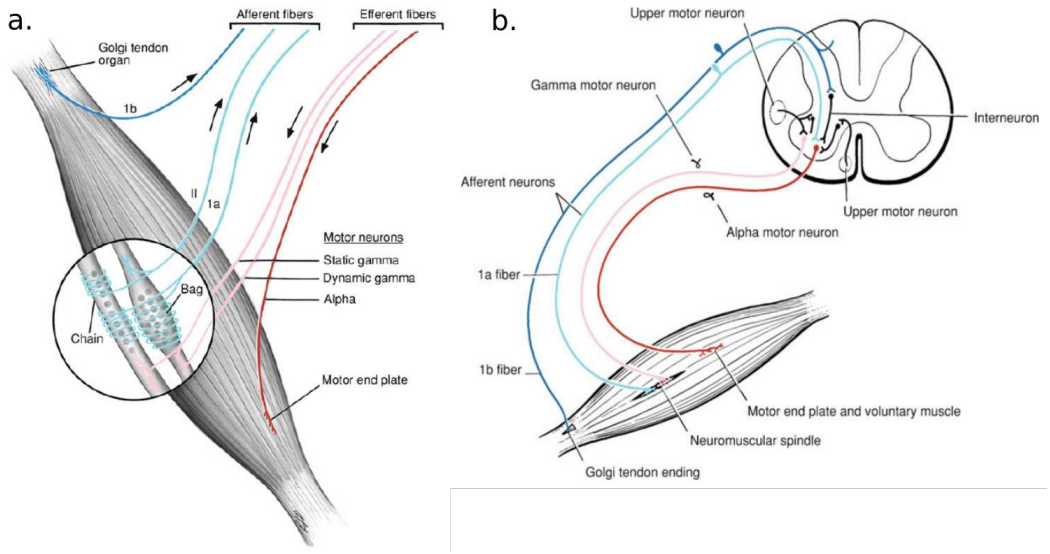

Figure 2.1. **a.** Type Ia, II, and Ib afferents together with efferents innervating muscle fibers. **b.** Afferent and efferent connections between a muscle and the spinal cord. Reprinted from [60] with permission (license number: 4275550297745). DOI:10.1007/978-1-61779-779-8_8

2.3.1 Neural reflexes and afferent feedback

One of the early studies to quantify effects of mechanical perturbations on control of walking used acceleration and deceleration impulses to measure changes in muscle activity during treadmill walking [61]. The study was designed based on the available knowledge at the time that during balance control as well as upper extremity movements humans showed responses to perturbations that consisted of three components named short latency, medium latency and long latency. The short latency component had a spinal origin. The medium and long latency responses origins were not clear (i.e., spinal vs. supraspinal). The acceleration used was a step increase in velocity from 4 to 9 km/h over 70 msec and deceleration was a decrease from 4 to 1.5 km/h over 60 msec. These impulses were delivered at the time of heel strike. The deceleration caused the body to sway backward with

an inhibition of GAS muscles on the ipsilateral leg and activation of TA on the contralateral side. Latencies of these responses in both legs were 65–70 msec. The acceleration, on the other hand, caused the body to sway forward and resulted in excitation of GAS in the ipsilateral leg and TA in the contralateral leg. The latencies were similar to the deceleration condition. The authors concluded that polysynaptic spinal pathways were responsible for conveying these responses since the latencies were too long for the involvement of monosynaptic pathways and the latencies were similar on both legs. Also, the possibility of any cortical involvement was rejected on the basis of the latencies being too short for transcortical modulations. Another study performed by this group around the same time [62] applied similar treadmill impulses as well as stimulation of tibial nerve to better investigate which pathways were involved in muscle responses. It was observed that stimulation of tibial nerve caused plantarflexion in the ipsilateral leg, which was followed by activation of TA. However, the strength of response from TA was dependent on the phase at which the stimulation was delivered with the early stance and the swing phases showing the most prominent responses. The latencies were around 90 msec. These responses were unchanged when ischemic nerve blockade of group I afferents was applied. It was concluded that group II afferents were responsible for modulation of observed responses. Also, the authors suggested that the early ipsilateral responses were likely responsible to correct foot and leg placements while the early contralateral and the late ipsilateral responses compensated for the body displacement.

Although the two studies mentioned above were performed more than three decades ago, they raised some of the most important questions related to responses of

the nervous system to mechanical perturbations of walking: How many components are present in the responses? Which pathways are responsible for modulation of each component? What is the functional role of responses in control of walking? To what extent the type of perturbation and walking conditions (speed, inclination, etc.) affect the responses? The studies that followed later tried to provide answers to these questions as well as some novel questions related to neural control of walking under mechanical perturbations.

A foundational study performed by Sinkjær et al. [63] investigated modulation of the short latency stretch reflex. The importance of their work relies on its elaborate discussion on neurophysiological characteristics of reflexes to mechanical perturbations. To quantify responses to perturbations Sinkjær et al. used a stretch device to apply torques to ankle joint during the stance phase. Subjects walked on the treadmill at speeds of 2, 3.5 and 5 km/h while perturbations of $7.5 - 10^{\circ}$ with stretch velocities of $220 - 270^{\circ}/s$ were applied. TA did not show any changes during the stretch. SOL showed responses with the onset latency of ~ 42 msec and peak latency of ~ 59 msec. These timings did not change with the phase at which the perturbation was applied. The amplitude, however, was the largest during stance while a complete suppression of reflexes was observed in the transition from stance to swing. It was concluded that the stretch reflexes depended on the amplitude and velocity of the applied stretch, the phase of the gait cycle at which the stretch was delivered and the walking speed.

Sinkjær group followed their previous work on short latency reflexes with a study that focused on long latency reflexes [64]. It was suggested previously that

stretch velocity-sensitive group Ia afferents were responsible for the short latency response (i.e., short latency reflex). However, the pathways involved in medium latency responses [1] and long latency remained unknown. This study measured these responses by applying ankle torques during stance and measuring EMG from TA and SOL and comparing them to sitting and standing. Subjects showed a short latency reflex with a peak latency of 50 msec which was followed by two long latency responses with peak latencies of 85 msec and 112 msec. Compared to walking no long latency component was observed during sitting and standing. Based on these results it was suggested that long latency component was part of a transcortical loop while short latency and medium latency components had spinal origins.

Although knowing the origin of different components involved in the stretch reflex during walking is important (e.g., for therapeutic applications), to understand how humans walk in face of perturbations requires us to identify the functional role of these reflexive responses in control of gait. Sinkjær et al. [65] explored the possibility of the feedback arising from stretch reflexes contributing to the regulation of walking. This was done by applying sudden unloading to plantarflexors during stance. In the first phase of experiment 6° unloading (i.e., plantarflexion) with a velocity of $330°/s$ was delivered and hold for 210 msec. In the next phase, the common peroneal nerve was blocked by injection of lidocaine. This was done to exclude the involvement of dorsiflexor in the modulation of responses. Finally, in the last phase, ischemic nerve block was induced in order to remove the short

[1] There is a lack of consistency in literature with regard to the naming convention for the medium latency component. Some studies call this component the medium latency response while others refer to it as a long latency reflex.

latency reflex. Unloading responses were observed in SOL followed by long latency responses in TA. Ischemia, however, did not result in major changes in responses which meant that sensory feedback from afferents other than group Ia was mainly involved in modulation of EMG during walking. Blocking of peroneal nerve also did not change the responses which excluded the possibility that reflexes were modulated through reciprocal inhibition of antagonist nerves. This suggested that the sensory feedback that controlled muscle activity during walking was perhaps modulated through group II or group Ib afferents.

Grey et al. [66] extended the role of group II afferents to modulation of spinal reflexes during dorsiflexion perturbations of the ankle. They used five different techniques to identify sensory afferents involved in responses. Using variable stretch velocities, nerve cooling, ischemia, tizanidine (an α2-adrenergic receptor agonist that suppresses the function of group II afferents) and local anesthetic depression of cutaneous afferent in the ankle, their study aimed to differentiate between the role of short and medium latency reflexes. They showed that unlike the short latency responses which were modulated by velocity sensitive group Ia afferents, the major contribution to medium latency responses came from group II and group Ib sensory afferents. Although their study could not differentiate between these two afferent groups and they could not exclude the possibility of an involvement from cutaneous afferents.

Nielsen and Sinkjær [67] made a distinction between two fundamental roles for sensory responses observed in previous studies. In one form the afferent feedback is integrated into motor programs directly as part of normal movements. The contri-

bution of sensory afferents to modulation of background EMG which was revealed through sudden unloading of plantarflexors falls into this category. The other role of sensory feedback is to convey the error signal from unexpected perturbations. The authors suggested the use of the word "reflex" should be reserved for the second role of sensory feedback. However, according to others [68,69] this distinction might not be necessary and it has been shown that in general the definition of reflex is not clear and researchers do not always state how they define it in their work.

Regardless of the conceptual differences between the unloading responses and rapid dorsiflexion perturbations, the neurophysiological differences and the individual pathways involved in each response had to be identified. Grey et al. [70] investigated the idea that afferent feedback involved in the enhancement of SOL EMG revealed by unloading responses was processed differently than the stretch reflex from rapid dorsiflexions. To achieve this goal they applied stretch and unloading perturbations to the same group of subjects and compared the responses for these conditions both during normal walking and after injection of lidocaine blocking cutaneous afferents of foot and ankle. They observed that dorsiflexion perturbations resulted in short latency (onset 32 msec) and medium latency (onset 78 msec) responses in SOL with no responses from TA while unloadings resulted in a SOL response (onset 55 msec) and a much smaller response of TA (onset 30 msec). The EMG responses did not show any differences after injection of lidocaine. These results provided evidence in support of unloading and dorsiflexion responses being modulated through different pathways. While the stretch responses are controlled through group Ia afferents, group II afferents are involved in the control of unloading

responses without any contribution from cutaneous inputs.

Although the study of reflexes in response to mechanical perturbations somewhat quantified the role of sensory feedback in control of muscle activity in lower leg muscles, the conclusions made in previous studies often relied on the application of rather large perturbations. Mazzaro et al. [71] addressed this limitation by applying perturbations that mimicked smaller deviations experienced in everyday walking. To achieve these conditions small dorsiflextion enhancements and reductions of about $\pm 5^{\circ}/s$ and $\pm 2^{\circ}$ were applied to the ankle joint with and without ischemia. In addition, the Achilles tendon was vibrated at 110 Hz during similar dorsiflexion perturbations to quantify the role of group Ia afferents. Dorsiflexion enhancements resulted in EMG increments of SOL muscle which were more sensitive to the velocity of the movement than the amplitude. While ischemia and Achilles tendon vibrations reduced these increments during dorsiflexion enhancements, they did not have any effect on EMG decrements during dorsiflexion reductions. This supports the involvement of afferent feedback in the modulation of SOL activity during small perturbations and suggests that SOL activity is sensitive to the feedback from group Ia afferents.

While many studies focused on the role of group Ia and group II afferents in the modulation of responses, the contribution of group Ib afferents from GTOs remained unexplored. Grey et al. [72] examined this contribution by modulating the feedback from GTOs using different inclinations ($\pm 4\%$) of the treadmill combined with rapid plantarflexion perturbations of the ankle during late stance. In all cases, a decrease in the activity of SOL and Achilles tendon force were observed. These

modulations increased as a function of treadmill inclination which showed that force feedback through excitatory group Ib afferents contributed to the enhancement of SOL activity during late stance. This outcome was further corroborated by the results of a following study from Klint et al. [73] for overground walking. Using a robotic platform they changed the inclination of the surface to apply small dorsiflexion and plantarflexion perturbations to the ankle joint in early stance. A significant contribution of their study was a second experiment which applied the same perturbations to a unique patient (IW) with complete lack of touch and proprioception senses [74]. In both SOL and GAS muscles of healthy subjects, the modulations of activities were increased with surface inclines and decreased with declines. IW muscle activity, however, did not show any changes with surface inclination.

To further quantify the effect of force feedback through sensory afferents on the control of walking, Klint et al. [75] designed an experiment which altered subjects' body weight during treadmill walking. A body weight support system was used to create variable body weights while subjects were walking on the treadmill during dorsiflexion and plantarflexion perturbations which were applied to the ankle joint in the mid and late stance. The perturbations were applied both in the normal condition and under influence of tizanidine which suppressed transmissions through group II afferents. The rationale behind this design was that if changes in muscle activity due to changes in the body weight happened through proprioceptive afferent feedback, then the response to perturbation should also change under these conditions since reflexes showed the amount of muscle activity generated by afferent feedback. This would allow us to differentiate between the role of muscle

spindles and the GTO feedback. The results showed that transient decreases in the body weight support led to increases in unloading response (to plantarflexion). Tizanidine which reduces group II afferent feedback did not result in any significant decrease in the unloading response. This suggests that the unloading response is more sensitive to the load feedback from group Ib than feedback from group II. It was also observed that the medium latency response was modulated by changes in body weight support but the short latency response stayed unaffected.

Not only the type of perturbation (e.g., dorsiflexion vs. plantarflexion) and the properties of the stimulus (e.g., stretch amplitude or velocity) affect modulation of responses through sensory afferents, but also specifications of the task such as the walking speed can alter afferent signals. Cronin et al. [76] applied dorsiflexion perturbations of three different stretch velocities to the ankle joint at three different walking speeds of 3, 4 and 5 km/h. They hypothesized that since at faster walking speeds muscle activity and muscle stiffness are higher, this will result in a decrease in the fascicle stretch velocity which could influence the amplitude of stretch reflex responses. Contrary to this assumption it was found that walking speed had no effect on the stretch reflex amplitude of the SOL muscle meaning that the spindle afferent feedback stayed the same at faster speeds even though the measured amplitude and velocity of fascicles stretch decreased with speed. This suggested some mechanisms had been involved in increasing the motoneuron output at faster speeds in order to prevent a decrease in the amplitude of the short latency stretch reflex. Although the nature of these mechanisms was not clear, the authors proposed this might involve a decrease in pre-synaptic inhibition at faster speeds or a combination of a decrease

in group Ia afferent feedback and an increase in the motoneurone drive.

2.3.2 Interlimb communication and crossed reflexes

Although the studies reviewed in the previous section have made significant contributions to advance our knowledge of the underlying mechanisms in the neural control of walking under perturbations, the mentioned studies have drawn their conclusions mostly based on the measurements from one leg. As a result, these studies have not investigated the neural couplings between the two legs that can lead to the interlimb communication which is necessary for maintaining coordination during recovery from perturbations. The interlimb communication often appears as crossed reflexes meaning that a perturbation to one leg can result in a neural response in one or more muscles in the other leg, which did not experience the perturbation directly. Figure 2.2 [77] shows a schematic of how a crossed reflex works. Upon feeling the stimulus in the right foot, sensory afferents carry the signal to the spinal cord, where through a polysynaptic pathway the motor efferents activate flexor muscles in the upper right leg and relax extensor muscles. This helps with lifting the leg (i.e., knee flexion) and minimizes the contact with the source of perturbation (e.g., a sharp object). Concurrently with this withdrawal reflex, the other leg has to accept the entire weight of the body to maintain a stable posture. To ensure this, at the same time that the sensory signals activate the interneurons of the right leg pathways, the efferent pathways of the left leg activate extensor muscles and relax the flexors. This straightens the left leg in preparation to carry the extra load.

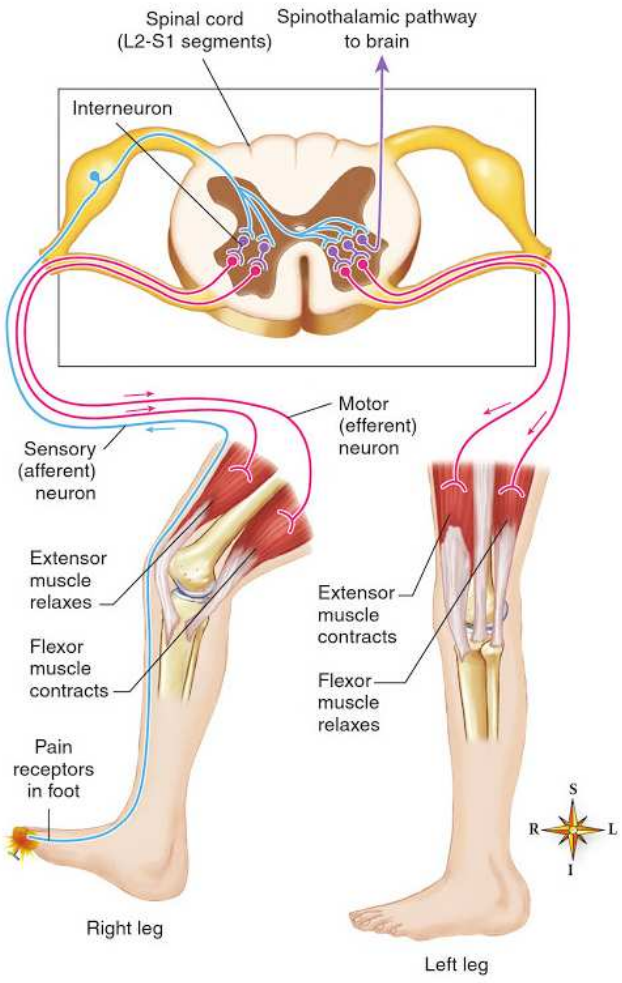

Figure 2.2. Example of a crossed reflex. Sensory and motor pathways and their connection sites in the spinal cord are shown for both legs. Reprinted from [77] with permission[a].

[a]This figure was published in Anatomy and Physiology, K. T. Patton, Figure 21-16, Page 496, Copyright Elsevier Health Sciences (2015), ISBN-13: 978-0323055321

The properties and functions of crossed reflexes during locomotion have been well documented in non-human mammals [78–80]. However, the role of crossed reflexes in human locomotion remained unexplored for a long time. Recently this phenomenon has gained more interest from researchers and several studies have investigated the characteristics of these reflexes and their roles in the control of

walking under perturbations.

Stubbs et al. [81] were the first to study the effects of ipsilateral nerves stimulations on the short latency responses of contralateral soleus. The ipsilateral tibial nerve (iTN) [2] was stimulated with different intensities at 60%, 70%, 80%, 90% and 100% of the gait cycle. In another setup, the ipsilateral sural (SuN) and medial plantar nerve (MpN) were stimulated at 90% of the gait cycle. Upon stimulation of iTN, responses were observed in the contralateral SOL with latencies of about 39.5 msec. The strongest responses occurred before and during the transition from the swing to the stance phase of the ipsilateral leg. At higher intensities of stimulation, responses became inhibitory at 80%, 90% and 100% of the gait cycle. No short latency responses were observed upon stimulation of SuN or MpN. This suggests that the reflexes in contralateral SOL originate from the afferent activity of the ipsilateral SOL and GAS not from the cutaneous receptors. The authors proposed that the functional role of the crossed reflex in SOL might be related to maintaining the stability during the late swing and the swing to stance transition phases. Since plantarflexion during the swing is detrimental to stability, it is likely that after the onset of perturbation, the ipsilateral muscles signal to contralateral leg to initiate an inhibitory response avoiding the progression toward the external source causing the instability.

Since the conclusions of Stubbs et al. only relied on the responses of SOL, Gervasio et al. [82] measured responses in GAS and compared that to the SOL

[2]Tibial nerve (iTN) is a branch of the sciatic nerve that innervates the lower leg and foot. It further branches off to the medial plantar nerve (MpN) and the sural nerve (SuN) which innervate the cutaneous receptors of the foot.

response. Additionally, with a novel experimental design they measured these responses during hybrid walking in which the right and left leg move in the opposite directions to investigate if crossed reflexes in humans are task specific. In their first experiment they applied electrical stimulation of the iTN to one leg and measured responses of contralateral SOL and GAS muscles during both normal and hybrid walking on the split-belt treadmill. Since the hybrid walking requires the contralateral leg to move in the opposite direction of the normal walking condition, this setup should result in a reflex reversal previously observed in animals [83, 84]. In a second experiment, they measured crossed responses to stimulation of SuN and MpN during both walking conditions. The iTN perturbation during normal walking created inhibitory short latency responses in contralateral SOL while it facilitated the contralateral GAS response. In hybrid walking the contralateral GAS activity was inhibited while the contralateral SOL did not show a significant response compared to unperturbed walking. This observed reversal of the GAS crossed reflex from normal to hybrid walking shows that short latency crossed reflexes are task specific. In the second experiment, while the stimulation of SuN and MpN did not show significant changes in GAS or SOL in normal walking, the statistical tests showed a significant difference between GAS and SOL responses of SuN and MpN stimulations and those of iTN. This suggests that unlike normal walking, cutaneous receptors provide important afferent feedback to control of hybrid walking.

To expand the investigation of crossed reflexes to other joints and the upper leg muscles, Stevenson et al. [85] explored the effect of the knee joint perturbation on interlimb communication. Previous research in animals [80] had shown that pertur-

bation of quadriceps and hamstrings elicited stronger crossed reflexes compared to the ankle muscles. So an experiment was designed to apply unilateral extension and flexion perturbations (mean angular displacement and velocity: $\sim 9^{\circ}$ and $\sim 302^{\circ}/s$) to the knee joint at multiple phases of the gait cycle. The study also included another experiment that took advantage of transcranial magnetic stimulation (TMS) to identify the neural origin of crossed responses. TMS was delivered before, at the same time and after the onset of cBF response. The ipsilateral knee extension evoked responses in cBF, cTA, and cSOL (mean onset latencies: $\sim 75 - 80$ msec) while the flexion perturbation did not result in any consistent contralateral reflexes. The lack of response from knee flexion was attributed to the perturbation not being strong enough to introduce the level of instability needed to initiate interlimb communications. While further research is required to confirm this argument, it is noteworthy to mention again that responses in the contralateral leg muscles (e.g., TA) have been observed previously [61] with perturbations in both directions. During the TMS trials, great facilitation of responses was observed when TMS signals coincided with the onset of response from cBF. This suggested that a transcortical pathway was involved in the formation of crossed reflexes in BF.

One possibility for the functional role of cBF reflex was to slow down the progression of the body to increase the stability as suggested by Stevenson et al. [85]. To confirm this hypothesis Stevenson et al. [86, 87] designed an experiment to suddenly change the treadmill speed in order to manipulate the need for stability at the same time the perturbation was delivered. If in fact, cBF reflex plays a role in maintaining stability, upon a decrease in the treadmill speed the amplitude of the

response should decrease. To test this, knee extension perturbations (mean velocity and amplitude: $\sim 293.5°/s$ and $\sim 7.6°$) were applied at 50% of the gait cycle while the treadmill speed was changed with accelerations of $\pm 5\ m/s^2$ which lasted for 1.5 seconds. The treadmill impulses were delivered relative to the knee extension onset ($-100, -50, 0$ and 50 msec). When the speed was decreased (increased) 50 or 100 msec before the perturbation it reduced (increased) the amplitude of responses and the combination knee perturbation and the change in speed resulted in responses more prominent than those observed in perturbation only trials. This showed for the first time that crossed reflexes in BF play a functional role in maintaining stability during walking under perturbations.

While the contribution of cortical pathways to crossed reflexes of BF was observed previously [85], it was not clear if the modulation of other muscle activations involved cortical control. Mrachacz-Kersting et al. [88] investigated this possible contribution to the crossed reflexes of GAS by stimulating the ipsilateral posterior tibial nerve (iPTN) at 80% of the gait cycle. What makes GAS to be the best candidate to identify cortical contributions to crossed reflexes is the characteristics of its crossed reflex which shows several peaks of activity in most subjects [82]. iPTN was combined with TMS perturbations delivered at different timings relative to the onset of iPTN. Subjects showed short (peak: $\sim$ 79 msec) and long latency (peak: $\sim$ 89 msec) crossed reflexes in GAS. The conduction time through a transcortical pathway for iPTN stimulation is estimated as 83 msec. The combination of iPTN and TMS showed significant suppression of the long latency crossed reflexes in GAS. This outcome and the latency of responses suggest transcortical pathways

are involved in modulation of the long latency component of the cGAS response.

2.3.3 Multijoint control under perturbations

The studies reviewed in the previous sections have provided a substantial knowledge of the underlying mechanisms involved in generation and control of reflexes during mechanical perturbations of walking. However, the aforementioned studies, as well as many others in the application of mechanical perturbations to human locomotion have mainly focused on the responses arising from perturbations of single joints such as the ankle or the knee. Human walking is a complex task that requires a large-scale coordination of many muscles and joints involved in the generation of movement. While single joint perturbations can be useful in certain applications such as the study of pathological gait where specific joints may show departures from normal patterns of activity, it is not clear if the results of single joint perturbations are generalizable to the whole body perturbations that humans often experience in natural environments. An alternative to single joint perturbation is the application of surface perturbation which elicits whole body movements and requires a multijoint control similar to what people show outside of laboratory conditions.

Chvatal and Ting [89] applied the surface perturbations of a custom build platform installed in the path subjects took while walking in a hallway. They hypothesized that muscle synergies could explain the modifications to walking under perturbation both in the reactive form in which subjects are not aware of the per-

turbation beforehand and in the voluntary form where subjects are told about the upcoming perturbation. The idea of muscle synergies states that the nervous system uses a few degrees of freedom to control high dimensional tasks such as walking by applying similar patterns of activity to groups of muscles. In other words, a few neural commands can control the whole movement by activating muscles in a synergistic way. These few neural commands are called synergies or motor modules [90–92]. A modular approach to control of walking using muscle synergies has been used before by some studies [93–96]. Chvatal and Ting used this approach and compared the synergies between walking at two different speeds, walking normally and under perturbations, and voluntary versus reactive modulations of walking under perturbations. In their experimental protocol, they applied sudden impulses to the platform in four directions of anterior, posterior, medial and lateral. Reactive responses were observed between 100 to 400 msec after the onset of perturbation and they were larger for anterior direction. TA and quadriceps showed responses to anterior while SEMT and GASm responded to posterior perturbations. They did not see major differences in muscle synergies used in walking between different speeds or between normal and perturbed walking. They concluded that voluntary, reactive and automatic tasks all use similar synergies. It is noteworthy to mention that contrary to the conclusion of Chvatal and Ting on similarity of synergies recruited at different speeds, two recent studies [97, 98] have shown that different synergies are used at different speeds of walking.

An issue with the methodology used in [89] is the technique used to apply mechanical perturbations to the foot. The application of a surface platform will allow

us to deliver the perturbations to only one step. Control of gait is a continuous process and the effect of perturbations can persist well beyond one step (e.g., phase resetting [99]). One way to bypass this limitation is to apply perturbations through velocity impulses in treadmill walking. Instrumented treadmills that can apply a wide range of velocity impulses have become more widespread in recent years and a few studies have used treadmill perturbations to explore responses of walking to mechanical perturbations. Sloot et al. [100] used treadmill acceleration and decelerations to measure stretch reflexes in calf muscles. At the speed of 1.2 m/s they applied accelerations and decelerations (up to 4 m/s^2) to the right leg that lasted 252 to 359 msec. These were delivered at 10 to 15% of the gait cycle ($\sim$ 147 msec after heel strike on average). No effect was observed on TA while all calf muscles showed responses to accelerations. The deceleration led to increased activity in TA and for some subjects in SOL while other calf muscles showed inhibitions. The delay in responses was in average 163 to 191 msec. The reported latencies were much longer compared to other studies discussed in previous sections and they do not fall in the interval usually reported for spinal reflexes. Sloot et al. expanded these results in a second study that applied similar perturbations to children with cerebral palsy [101]. The average muscle activity in response to accelerations of the treadmill compared to unperturbed walking was increased 3 and 3.5 times in healthy and cerebral palsy children respectively.

One difficulty in the approach used by Sloot et al. is that long discrete perturbations result in responses that are difficult to separate from ongoing effects of perturbation. For instance, if a change in the activity is observed 100 msec after

the onset of a perturbation that lasts 200 msec, it is not possible to know if this response is a long latency response to kinematic changes applied immediately after the onset, or a short latency response to changes that happened 50 msec after the onset. One way to avoid this limitation is to apply continuous perturbations. Moore et al. [102] used this approach to quantify responses to mechanical perturbations. However, their experiment only measured kinematic responses and EMG recordings were not included. A recent analysis performed on the data by Ehtemam et al. [103] has shown that perturbations resulted in kinematic responses immediately after onset of perturbation. A kinematic response establishes the relationship between the perturbation and the kinematic changes in the limbs and joints. The perturbation has to be large enough to result in significant kinematic changes above the noise level. However, it is not clear yet if these kinematic changes result in responses from the nervous system in form of changes in muscle activations. This is left to future studies to investigate.

2.4 Summary and future directions

This review discussed the most important findings of previous research related to control of walking in humans. Three major topics were covered. First, the knowledge available from the literature on the relationship between muscle activity and speed of walking was discussed. Most studies have focused on the effect of speed on modulations of muscle activity during steady-state walking. Study of this relationship under transient conditions during perturbations of gait has not received

much attention in the past. One way to replicate these transient conditions in a laboratory setup is the application of visual or mechanical perturbations.

The second topic covered was the effects of visual perturbations on control of walking. Visual perturbations can alter the perception of speed (and other gait parameters) which in turn can result in subjects changing their muscle activity in a transient fashion to modify their gait. As it was discussed, previous research has shown that humans use the optic flow in control of walking and modulations they apply depends on the properties of the flow such as velocity, texture density, the location of objects, etc. With an increase in optic flow people usually slow down and a decrease in optic flow makes them walk faster. These effects are more prominent at lower speeds as control at higher speeds of walking involves a larger contribution from automated motor programs rather than sensory feedback.

Lastly, the effects of mechanical perturbations during walking was discussed. The latencies of responses to perturbations and their neural origins have been extensively studied. It is believed that velocity-sensitive group Ia afferents are involved in the short latency stretch reflex. Group Ib and group II afferents contribute to medium latency responses as well as modulation of the background muscle activity during walking. Some studies have suggested that transcortical input plays a role in modulation of long latency reflexes and the involvement of cortical pathways in the initiation of crossed reflexes have been demonstrated using TMS perturbations.

A major gap in the literature to understand control of speed during walking is related to the fact that majority of studies have looked at muscle activations during steady-state conditions of walking and the few studies that have examined walking

under transient conditions have not measured muscle activations under those conditions or for transient responses of walking under perturbations. Another gap that currently exists is related to the size of changes in speed or muscle activations under study. Previous research has looked into the relationship between large changes in muscle activations and large changes in speed. To put this into perspective, the natural ankle angular velocity during walking is in the order of $20°/s$. However, most perturbations applied to the ankle has used the stretch velocities an order of magnitude larger than the values for normal walking. An important role of the nervous system as the controller is to maintain the desired speed under small constantly occurring perturbations from the environment. It is not clear how control strategies and changes in muscle activations for this task are compared to large changes studied in the past. Additionally, different studies have applied perturbations at different phases of the gait cycle. This makes it hard to compare the results across different studies and to aggregate the findings into one coherent story. The studies in this dissertation (i.e., the following chapters) are designed to address these gaps in the literature. Small continuous visual and mechanical perturbations are applied to quantify the dynamics between the plant and the neurofeedback while people control their speed of walking on the treadmill.

3

Visual perturbations and changes in muscle activity

There are two possible outcomes: if the result confirms the hypothesis, then you've made a measurement. If the result is contrary to the hypothesis, then you've made a discovery.

Enrico Fermi

Nobel laureate in Physics 1938

3.1 Introduction

The speed of walking is a function of the kinematics of limbs which in turn are determined by the forces generated in muscles through the application of the laws of motion from Newtonian mechanics. The movement is actively controlled by the motor commands generated in the central nervous system and sent to the musculoskeletal system through the efferent pathways. These motor commands can be estimated with the electrical activities in the muscle tissue, which are recorded using electromyography techniques. Activities of muscles as a function of time, also known as muscle activations provide information on how the motor commands change in order to control the movement of the limbs and achieve the desired goal, in this case, a certain speed for walking. To study these changes, in this chapter we propose an experiment that elicits transient changes in muscle activations through the application of perturbations in a virtual reality environment.

3.1.1 Research question

The transient responses of muscles to rotation of the visual scene described in a recent study [19] showed that subjects decreased their plantarflexors activities in mid-stance in order to increase their speeds in response to visual perturbation. The current knowledge available from the literature on steady-state walking does not report any decreases in plantarflexor activity with an increase in speed. This study seeks to systematically examine this transient pattern of activity by comparing transient changes in muscle activations in response to small visual perturbations to

small differences in muscle activations between walking at two steady-state speeds.

3.1.2 Specific aims

Aim #1: To address the gap in the literature from steady-state walking studies and expand upon the previous work by identifying the transient changes in muscle activations and their relationship to kinematic changes and compare those to the changes between two steady-state walking conditions. In other words, we want to compare the changes in the average activity due to a change in steady-state speed to changes observed during transient responses to perturbations. We will use a system identification approach [19] to derive muscle activation profiles for perturbed trials and repeat the analysis using the steady-state averaging method and then compare the results to normal walking trials to demonstrate the differences.

Aim #2: To determine the role of lower leg muscles in control of speed from the changes measured between steady-state walking conditions and compare that to their role during transient responses described before [19]. Hypothesis: Based on the available knowledge from the literature [19] we hypothesize that plantarflexor muscles provide the main impulse required to increase speed. We predict this increase in the activity to occur as a response to perturbation received during the stance phase of the cycle before the peak of activity of the plantarflexors at push off.

Aim #3: To compare the mean waveforms of activity between steady-state walking and transient responses. We hypothesize that after averaging muscle acti-

vations over all gait cycles for each condition to obtain mean waveforms, the mean waveforms for the steady-state and perturbed conditions will be similar. We make this prediction based on the fact that the applied perturbation is small.

3.2 Methods

3.2.1 Subjects

The experimental protocol was approved by the Institutional Review Board (IRB) at the University of Maryland. Twenty-one healthy subjects (12 females) between the ages of 18 and 30 (mean: 21.7) with no neurological disorder participated in this study. The testing procedure was explained to the participants and their written consent was obtained prior to experiments.

3.2.2 Apparatus

The virtual reality environment consisted of a large translucent screen with the width and height of 244 cm and 305 cm. The visual scene consisted of 500 randomly positioned small triangles on a dark background (Figure 3.1) projected to the screen in front of the subject at a frame rate of 60 Hz by a JVC projector. In the middle of the screen in front of the subject at the eye level was a small no-triangle region of 30-cm-radius, which the subject was asked to focus on during walking. A fixed perspective point was defined at the eye level and 109 cm from the screen. The virtual movements of the visual scene were generated using CaveLib software (Fakespace). During the trials, the room was made completely dark so that the only

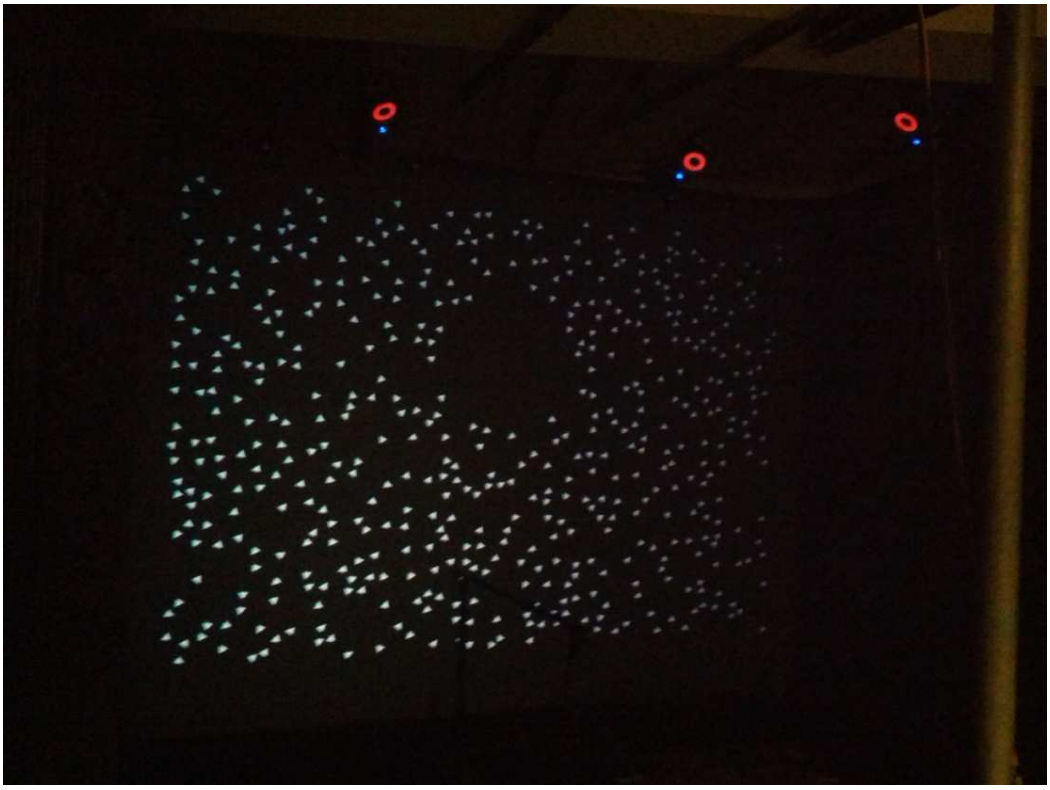

Figure 3.1. The large screen in front of the treadmill where the visual perturbation is projected. Some of the infrared cameras above the wall are visible in this picture.

visual information available to the subjects came from the screen in from them.

A motion capture system consisting of ten infrared cameras (VICON Inc., Oxford, UK) and reflective passive markers (diameter: 1.4 cm) was used to record kinematic data. The markers were attached on both sides of the body on the following anatomical landmarks: lateral malleolus (ankle), lateral femoral condyle (knee), greater trochanter (hip), iliac posterior, scapula at the level of T4 vertebra, elbow and wrist. Two markers were attached to the shoes where the posterior calcaneus (heel) and the 5th metatarsal (small toe) were located. Subjects wore a pair of goggles during walking and two markers were attached to the goggles to track the head motion. Data was recorded at a sampling rate of 120 Hz.

Muscle activity was captured through surface EMG using a wireless 16 channel TRIGNO system (DELSYS, USA). Fourteen muscles on the right side of the body were recorded: tibialis anterior (TA), soleus (SOL), gastrocnemius lateralis (GASl), gastrocnemius medialis (GASm), rectus femoris (RF), vastus lateralis (VASl), vastus medialis (VASm), bicep femoris (BF), semitendinosus (SEMT), tensor fascia latae (TFL), gluteus medius (GLmed), gluteus maximus (GLmax), lumbar erector spinae (ESL), thoracic erector spinae (EST). The belly of each muscle was located according to SENIAM guidelines [104] and the recording site was cleanly shaved and abraded with alcohol swabs. Data was recorded at the sampling rate of 2400 Hz.

3.2.3 Perturbation

Filtered white noise was used as the perturbation signal specifying the anterior-posterior position of the visual scene. Based on previous studies (e.g., [19]) we expected forward and backward movement of the visual scene to increase and decrease, respectively, walking speed, presumably because movement of the visual scene is interpreted by subjects as self-motion. To create perturbation signals, white noise with a spectral density of 1500 cm^2/Hz was low-pass filtered at cutoff frequencies of 0.02 Hz and 5 Hz using first-order and second-order Butterworth filters, respectively. The length of each perturbation signal was 250 seconds and the first and last 5 seconds were multiplied by a ramp function to ensure the perturbation amplitude started and ended at zero.

3.2.4 Protocol

Before data collection started, subjects walked on the treadmill in front of the screen to familiarize themselves with the experiment setup. Subjects were instructed to maintain an upright posture for head and torso and to only look straight at the screen while walking. Two treadmill speeds of 1.25 and 1.39 meters per second (2.8 and 3.1 miles per hour) were used. Speeds were chosen from a range (1.2–1.4) that contains the preferred speed of walking for most people [105–107]. Difference in speeds was chosen in a way that it is large enough ($\sim 10\%$ increase in the speed close to the preferred speed of walking) to result in an observable change in the average muscle activity for steady-state walking but it is small enough that does not result in drastic changes in transient patterns of activity. At each speed, subjects walked for eight trials with each trial lasting 250 seconds. The first and last trials captured unperturbed walking while the other six trials recorded transient responses to visual perturbations. Subjects were given the option of taking breaks in between trials as they needed. The order in which speeds were instructed was alternated between subjects, meaning that half of the subjects walked at the faster speed first and the other half second.

3.2.5 Analysis

Data processing. Kinematic data was low pass filtered at 20 Hz to remove noise. The EMG signals were high pass filtered at 20 Hz to remove movement artifacts and then rectified. The recorded signal from each trial was partitioned

using estimated phase (see below). The gait cycle starts at the phase of zero and ends at 100%. For each subject and muscle, EMG signals were averaged over all cycles and then over all trials to obtain a mean waveform. The RMS of this mean waveform was then used to normalize the EMG signals for that subject and muscle. For each of the four conditions (perturbed and unperturbed walking at each of the two speeds), normalized EMG signals were averaged across cycles, trials and subjects to obtain the mean waveform for that condition. Figure 3.2 shows the MWs of soleus for unperturbed conditions at two speeds. We will refer to the change between the activities at two speeds as the MW change and calculate it by subtracting the activity at lower speed from the activity at higher speed. This means that a positive change represents the amount of muscle activity required to increase the average speed for steady-state walking from the lower speed to the higher one.

System identification. We used a system identification approach developed in a recent study [19] which will be reviewed here briefly. In linear time invariant (LTI) systems the relationship between the input and the output can be described in the frequency domain through frequency response functions (FRFs). In these systems, an input with the frequency of f_1 creates an output at the same frequency f_1. The gain function of FRFs is the ratio of the input amplitude to the output amplitude and the phase function describes the temporal shift (relative to the cycle period) between the input and the output (i.e., lead or lag). Gain and phase are functions of frequency. FRFs estimations can be converted to the time domain to form impulse response functions (IRFs). If through experimental measurements we estimate the IRF for a linear system then for any given input $v(t)$ of the system the output $u(t)$

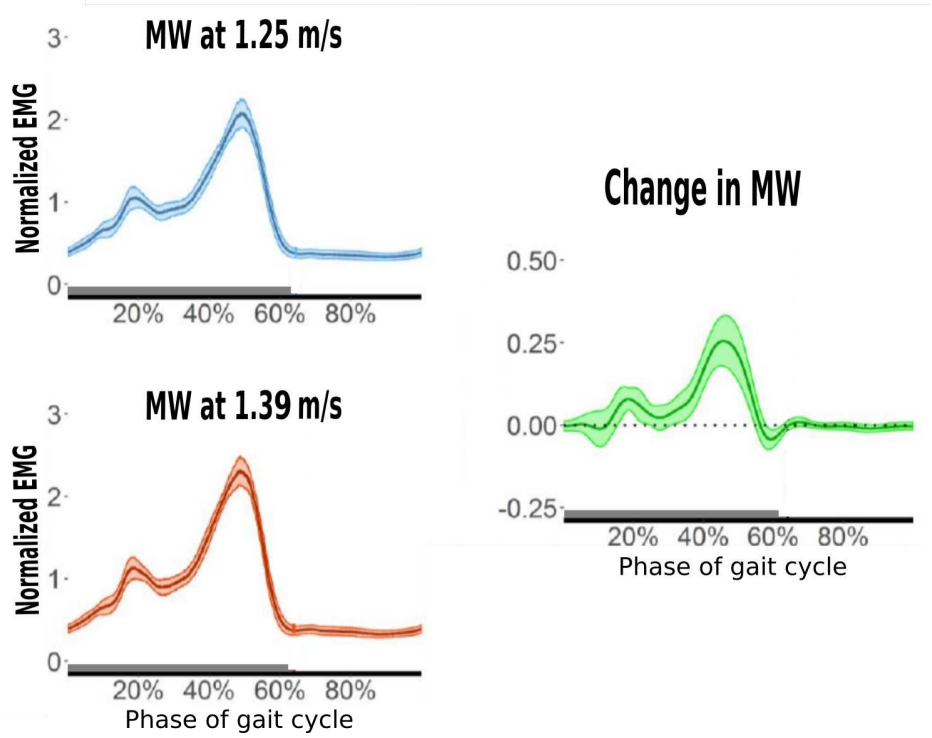

Figure 3.2. Mean waveform (MW) of activity for soleus at each speed (left) and the change in MW from the lower speed to the higher speed (right). The blue curve is MW at 1.25 m/s and the red curve is MW at 1.39 m/s. The shaded areas are 95% confidence intervals. The horizontal axis is phase of the gait cycle. The vertical axis is normalized muscle activity. The grey bar on horizontal axis marks the stance phase.

can be estimated using the IRF:

$$u(t) = (v * h_{vu})(t) = \int_{-\infty}^{t} v(\tau) h_{vu}(t - \tau) d\tau$$

In mathematical terms, the output is a convolution of the input and the IRF where convolution as an operator is shown with the $*$ sign. In the equation, h_{vu} is the IRF from the input $v(t)$ to the output $u(t)$.

Rhythmic systems like locomotion with a stable limit cycle, however, are not LTI. When perturbations from the environment are small, these systems can be

described by a local limit cycle (LLC) approximation. However, in general, an LLC system may not be perfectly periodic. In human locomotion, for instance, the walking rhythm can be advanced or delayed in response to external perturbations, a behavior called phase resetting [99]. In presence of perturbations, the IRF of the system depends on the phase of perturbation. We refer to this phase-dependent IRF as a φIRF, where φ denotes phase. The response of an LLC system to perturbations has two components: a transient component, which for human walking usually fades away after one or two cycles, and the phase resetting component. Both components of the response for the input $v(t)$ and the output $u(t)$ can be written as:

$$u(t_r) - u_0(t_r) = \int_{-\infty}^{t_r} h_{vu}(t_r, t_p) v(t_p) dt_p$$

Where t_r is the time of the response, t_p is the time of perturbation, u_0 is the unperturbed periodic output and h_{vu} is the φIRF.

We change the independent variable from time to estimated phase so that we can use existing LTP methods to estimate the φIRF. If $t_1, t_2, \ldots, t_k$ are the heel-strike times of k cycles in a trial we define phase as $\theta_d(t) = k + f_0.(t - t_k)$ where f_0 is the average frequency for that trial and θ_d is a discrete approximation of phase for $t_k < t < t_{k+1}$. We then use a second-order low pass filter to obtain a continuous estimation of the phase. Using this estimated phase as the independent variable, we can consider the system as LTP and calculate a φIRF to characterize the system. To perform the calculations in an easier way we use frequency domain analysis since convolution in the time domain is multiplication in the frequency domain. While

analysis of an LTI system in frequency domain results in FRFs, analysis of an LTP system in frequency domain provides us with harmonic transfer functions (HTFs). The theory of HTFs was initially developed in aerospace and electrical engineering to be used in industrial applications [19,108,109]. Here we apply this theory to human locomotion and calculate HTFs for responses to visual perturbations. We then transfer HTFs to the time domain and present φIRFs for all phases of perturbation. We add a correction term to the φIRF so that, to first order, the calculated φIRF does not depend on the method used to estimate phase.

Data visualization. Before we present the results in the following section, here we explain how to read the graphs we have made for visualizing the transient changes and phase resetting from these experiments. Figure 3.3 shows phase dependent IRFs for the soleus muscle which is a plantarflexor. The figure depicts changes in the IRF as a function of the phase of perturbation and normalized response time. The phase of perturbation refers to the phase of the gait cycle (e.g., toe-off time) at which the perturbation was applied. The amplitude of the IRF also depends on the normalized response time, the phase at which the response (i.e., change in muscle activation or kinematics) is measured. Since inspecting 3D plots is difficult for human eyes and we have many graphs to present, we will project 3D plots into the 2D plane and use color to represent the third dimension (i.e., amplitude of IRF).

Figure 3.4a is the 3D data mapped into 2D using a heat map. The horizontal axis shows the phase at which the perturbation is presented to the subject. The heel-strike on this axis is at zero, which is in the middle of the axis. The reason for this is to have a better representation of the responses since important parts of response in

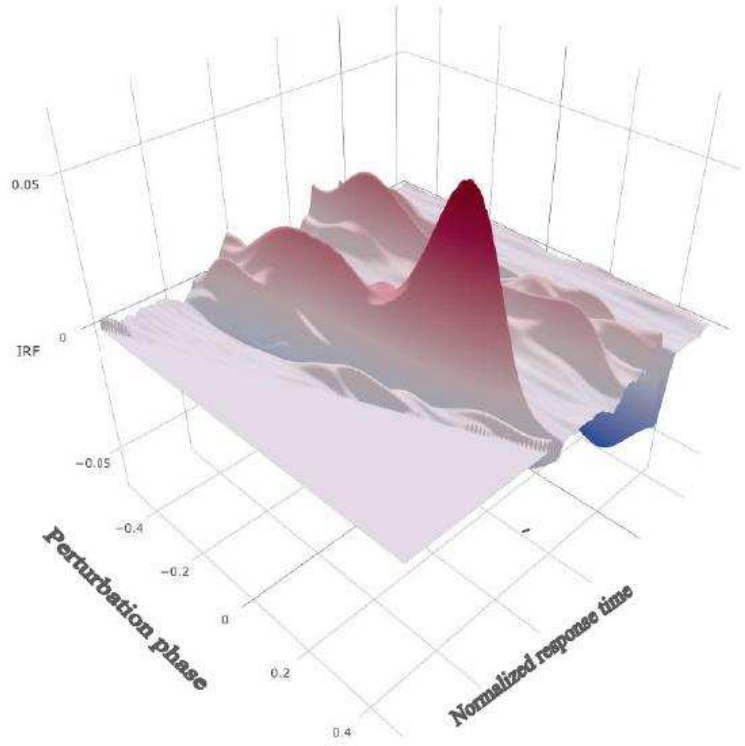

Figure 3.3. Three dimensional plot of transient muscle activity for soleus. The vertical axis is the values for impulse response function (IRF). IRF is a function of phase of stimulus and phase of response (i.e., normalized response time). These variables create a surface in 3D space.

some muscles happen around the heel-strike so instead of starting the axis from zero and ending it at one, the axis starts at -0.5 and ends at 0.5. The gray band above the axis marks the stance part of the gait cycle so before the heel-strike (zero on the axis) the leg is in the swing. The vertical axis shows the phase of the response. Here again, the gray bands mark the stance part of the cycle. The first cycle of response starts with the heel-strike at zero and ends with the next heel-strike at one. The color represents the values from the third dimension (i.e., IRF magnitude). To improve readability of the graph a diverging color scheme [110, 111] is created in which red represents positive values (i.e., increase in the activity when the scene moves toward the subject) and blue represents negative values (i.e., decrease when the scene moves away). Since the system is causal we do not expect to see a response before the onset of perturbation (i.e., region below the diagonal). Any line parallel to the vertical axis shows a slice of IRF (i.e., slice of the contour in 3D space). We have marked the slices with the highest and lowest IRF values during the first cycle (Figure 3.4b). As we can see these graphs are similar to the steady state graph presented in Figure 3.2. The difference is that these graphs represent the transient change in muscle activity after perturbation was applied. We call this transient change in the waveform (TW) and we will compare it to changes in MW.

The contour plot in Figure 3.4a is the average of transient activity at two speeds (1.25 m/s and 1.39 m/s). We average the transient activity because as part of Aim#1 of this study, we are interested in the similarities between changes in MW (Figure 3.2) in a range of speed and the transient waveform (TW) in that range. As it can be seen in Figure 3.5 the TW of a sample muscle shows very similar patterns

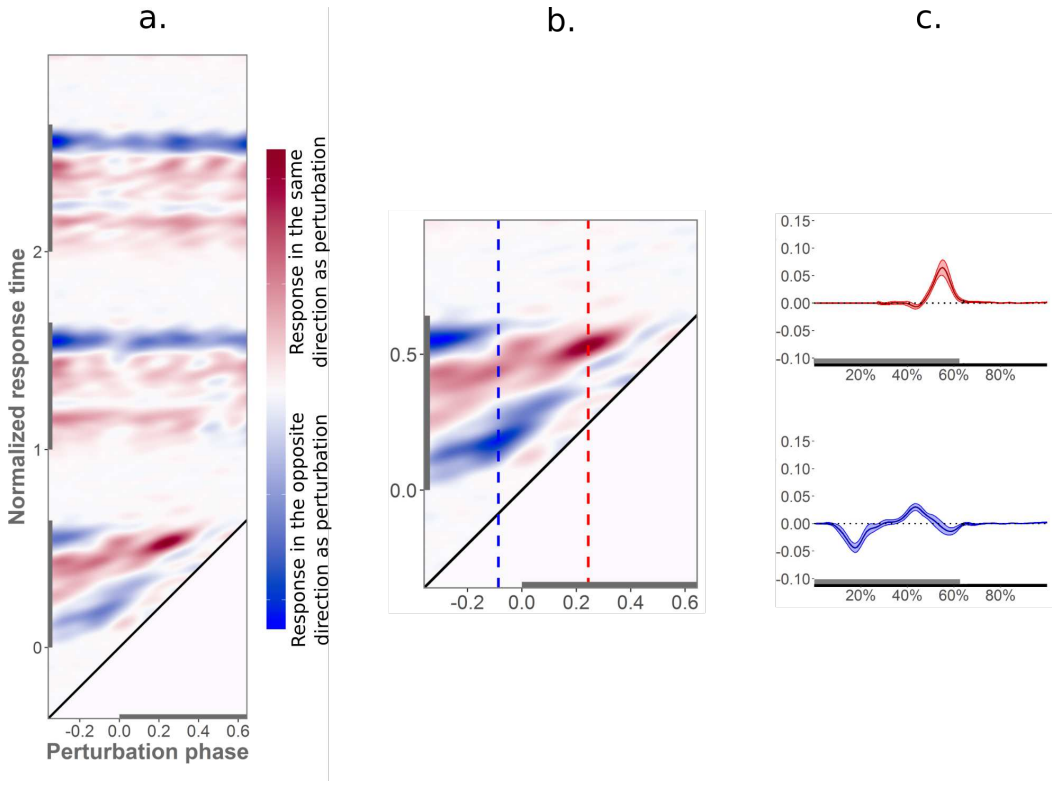

Figure 3.4. **a.** φIRFs for SOL showing responses for three cycles following perturbation. The grey bars on axes mark the stance phase. **b.** Responses from the first cycle highlighted. Each slice of the 2D plot is an IRF for a specific phase. The blue and red dashed lines mark two slices of interest. **c.** Slices that correspond to the highest (dashed red from **b**) and lowest (dashed blue from **b**) levels of activity. The shaded areas are 95% confidence intervals.

at the two speeds. All data presented for TWs in the following sections will be averaged data between the two speeds.

Statistics. To test the hypothesis that averaging over gait cycles for responses does not result in a statistically significant mean waveform than the average mean waveform of unperturbed trials, the area under activation profiles were compared between the unperturbed and perturbed conditions. Student t-tests were used to show that averaging the activity over all cycles results in insignificant differences between steady-state and transient conditions (Aim #3). $p<0.05$ was considered

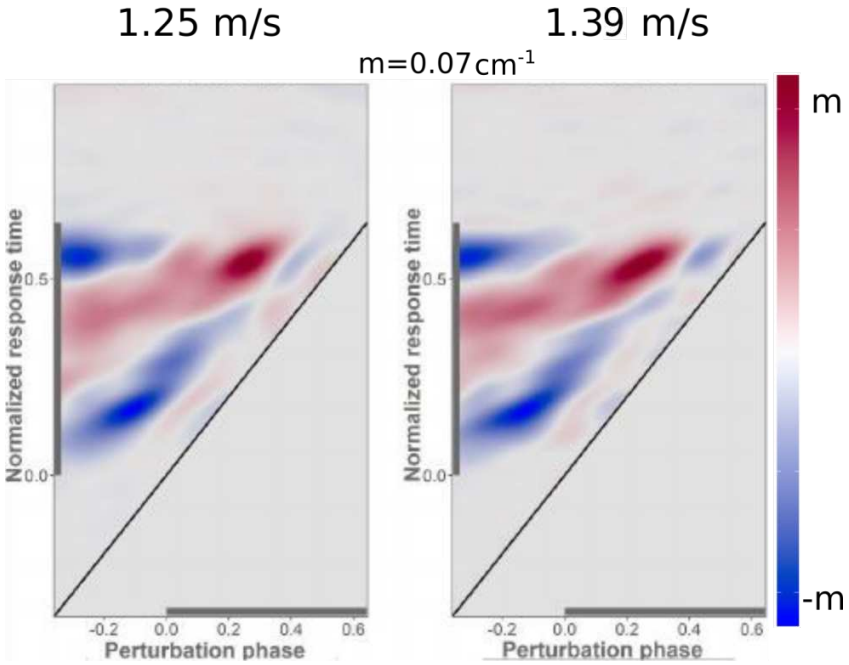

Figure 3.5. Transient activity of SOL at two different speeds. The grey bars on each axis mark the stance phase of the cycle where zero corresponds to heel-strike.

significant. Calculations were performed for the dorsiflexor and plantarflexors.

For both steady-state and transient profiles 95% confidence intervals were constructed. In the areas where confidence intervals include zero, the steady-state or transient activity is not significantly different than zero. To adjust the p-values and control the family wise error, the tmax method [112] was used for kinematic data. The method used bootstrapping (100000 bootstrap samples) to calculate p-values defined based on the maximum value of φIRFs. This determined if the φIRF that was averaged across all subjects was significantly different than zero or not. If the averaged φIRF for a muscle is significantly different than zero then the slices of the φIRFs for that muscle can be used for analysis. A modified version of the tmax method was used for EMG data. In this method we used the maximum absolute value of the EMG signal instead of the maximum absolute t-value.

To address the first aim of this study, we want to examine whether an increase in speed is always associated with decreased plantarflexor activity during mid-stance. Therefore, we want to compare transient plantarflexor responses to visual-scene movement to changes in steady-state plantarflexor activity caused by a change in treadmill speed. However, these two changes in plantarflexor activity have different units, so we normalize by the maximum change in each case to allow for a direct comparison. To do so we divide the absolute value of the largest decrease in the activity to the largest increase for both TW and changes in MW. We then calculate the difference between the two and call it the difference in negative to positive ratio (dNPR) described as:

$$dNPR = \frac{|min(TW)|}{max(TW)} - \frac{min|(\Delta MW)|}{max(\Delta MW)}$$

The $min(TW)$ is the minimum of the slice that contains the overall most negative response (third row in Figure 3.9) and the $max(TW)$ is the maximum of the slice that contains the overall most positive response (second row in Figure 3.9). The $min|(\Delta MW)|$ is the minimum of the absolute value of the change between the two mean waveforms (first row in Figure 3.9) and the $max(\Delta MW)$ is the maximum of the change between the two mean waveforms (the peak in the first row in Figure 3.9). A positive value for dNPR shows that transient changes have a significantly larger decrease in activity during the first half of stance compared to steady-state walking. We use percentile-t bootstrapping [113, 114], to examine whether dNPR is significantly above zero. All statistical analysis was performed in R [115].

3.3 Results

Figure 3.6 shows φIRFs for all muscles. A φIRF describes the response to a small brief perturbation (an impulse) applied at any phase of the gait cycle and, by extension, the response to any small perturbation. We inferred these responses to impulses based on responses to broadband continuous perturbations (see Methods). We saw statistically significant responses for all muscle groups. Figure 3.6 (top right) shows that when the visual scene moves forward during mid-swing, TA activity increases immediately after heel strike. This is the change in the activity compared to the mean waveform (signal depicted in green) since the mean waveforms were subtracted from the signals before we calculated φIRFs. When the visual scene moves forward during early stance, plantarflexor activity increases in late stance. As plantarflexors, these muscles are responsible for generating the propulsive forces necessary for increasing speed [116]. For all muscles we observed responses similar to those reported before [19]. The changes in the activity for BF, GLmax and EST were not significant (p-value>0.05).

Since previous studies [24, 117] have shown that the contribution of SOL and GAS to body support and forward progression is more than all other muscles combined we will focus our comparison of changes in the mean waveform and transient responses to the lower leg muscles. Figure 3.7 shows a better view of responses for TA, SOL, GASl and GASm with the slices with the highest increases and decreases in activities marked. These slices are shown and compared to MW changes in Figure 3.8 and Figure 3.9.

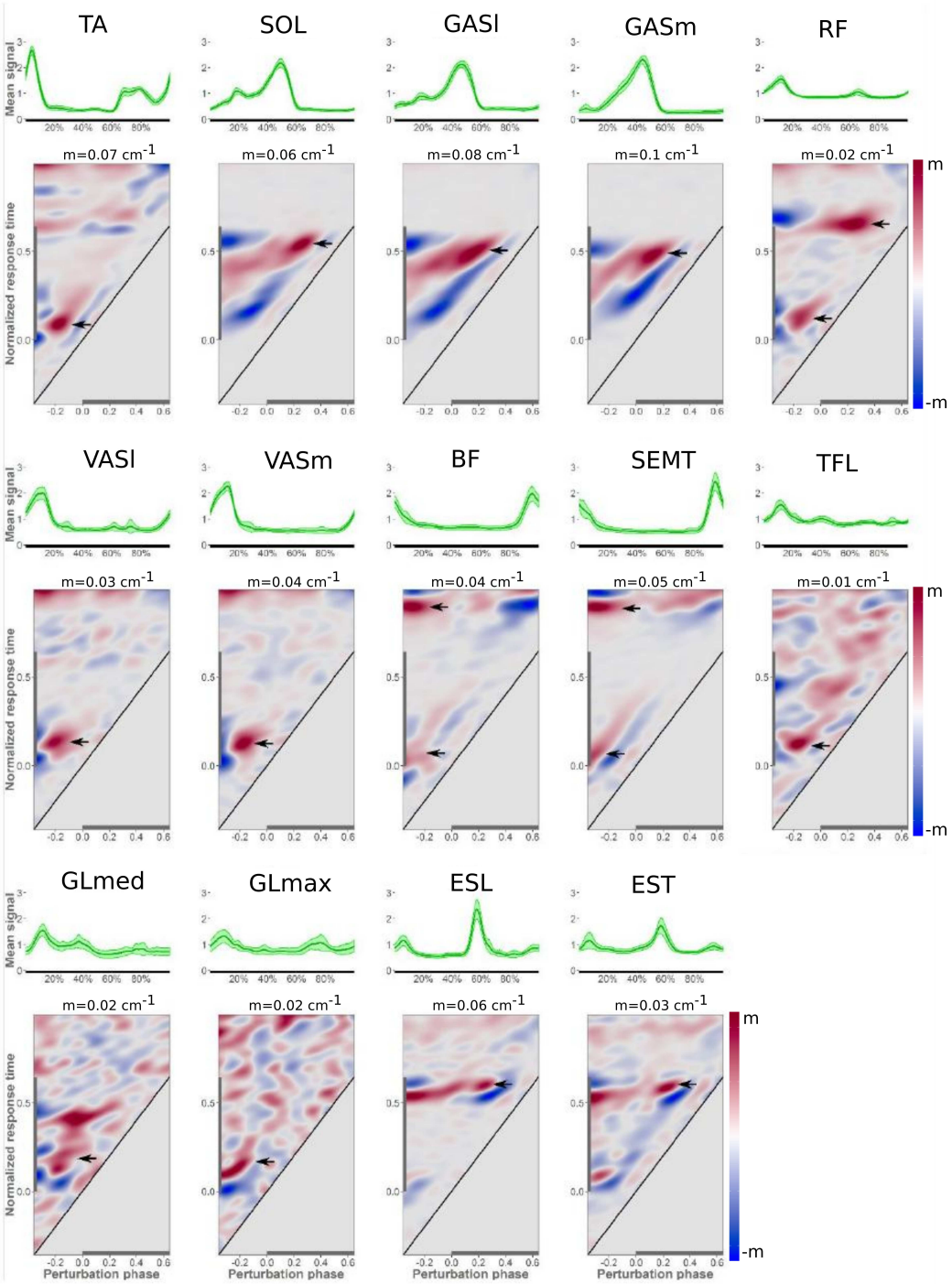

Figure 3.6. φIRFs for fourteen muscles during the first cycle after perturbation. The plots on top of φIRFs show mean waveforms. The shaded areas show 95% confidence intervals.

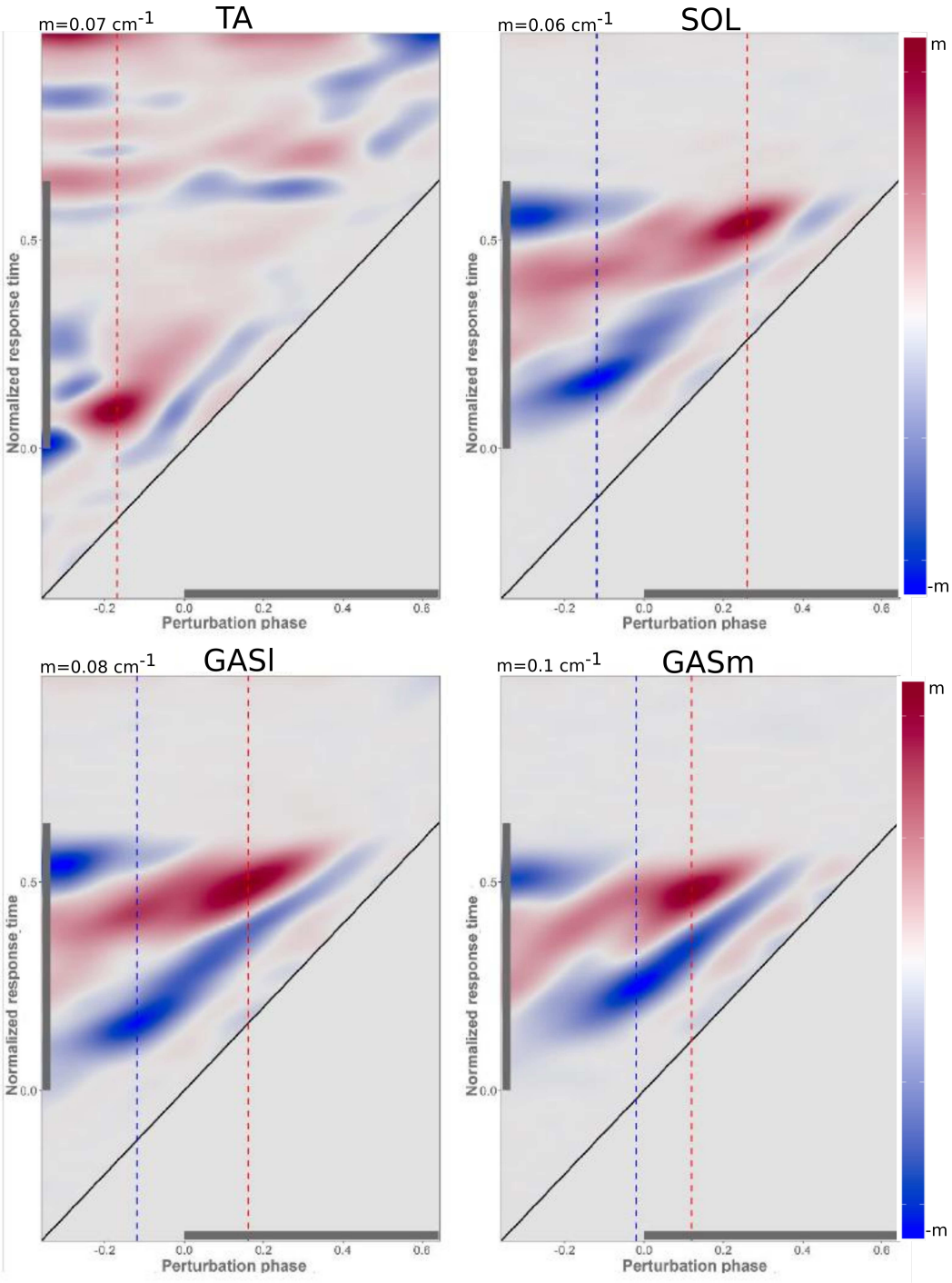

Figure 3.7. φIRFs for a dorsiflexor (TA) and three plantarflexors (SOL, GASl and GASm)

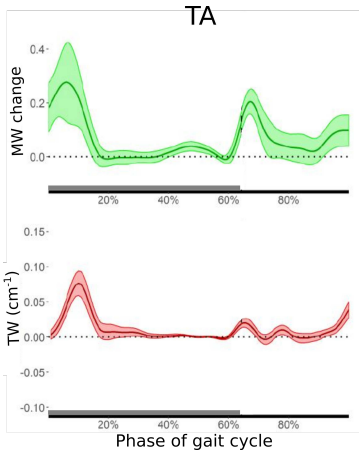

Figure 3.8. Comparison of transient waveform (TW) to mean waveform (MW) changes for TA. Transient activity here is from the slice marked with red dashed line in figure 7. This slice correspond to the largest increase in transient activity in response to perturbations applied during late swing.

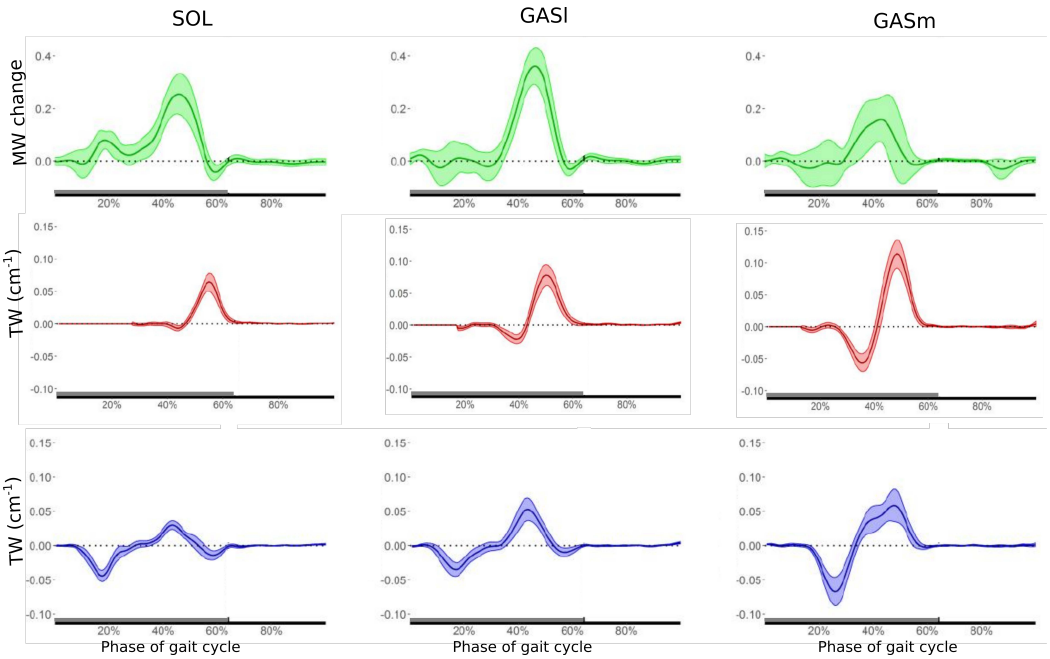

Figure 3.9. Comparison of TW (i.e., slices of IRFs) to MW changes for plantarflexors. Transient activity in the second row is from the slices marked with red dashed lines in figure 7. These slices correspond to the largest increase in activity in response to perturbations applied during early stance. Transient activity in the third row is from the slices marked with blue dashed lines in figure 7. These slices correspond to the largest decrease in activity in response to perturbations applied during late swing.

As we can see in the figures there are similarities between the two signals for all muscles. TA shows an increase in the activity after heel-strike and plantarflexors show increased activations before toe-off. This is in agreement with results reported before [19]. However, there is also a major difference between the two signals observable in plantarflexors activations. Prior to the period of increased activity in preparation for push off, there is a significant decrease in the activity that exists in TW patterns but is absent from MW changes. A closer look at the contour plots of plantarflexors (Figure 3.7) reveals that the center of this decrease happens at a perturbation phase before the heel-strike (i.e., perturbation is received during the swing). Slices from the center of this event for the three plantarflexors are shown and compared to MW changes in Figure 3.9.

As the figure shows (third row), there is a significant decrease in transient activity due to the perturbation during the first half of stance; a change that is absent in steady-state walking (first row). To test whether this decrease in TW is significantly larger than any decrease in MW changes we calculated dNPR (see Methods) for the three plantarflexors, which is positive if this case is true. The results showed dNPR values to be significantly above zero for all muscles. For SOL, GASl and GASm 95% confidence intervals were 0.25–0.8, 0.12–0.46 and 0.07–0.65 respectively.

Forward movement of the visual scene resulted in the transient modulations of muscle activations we have just described. The total effect of the modulations of activations of all muscles (those we recorded from as well as those we did not) was a transient increase in walking speed. We quantified the effect of perturbations on

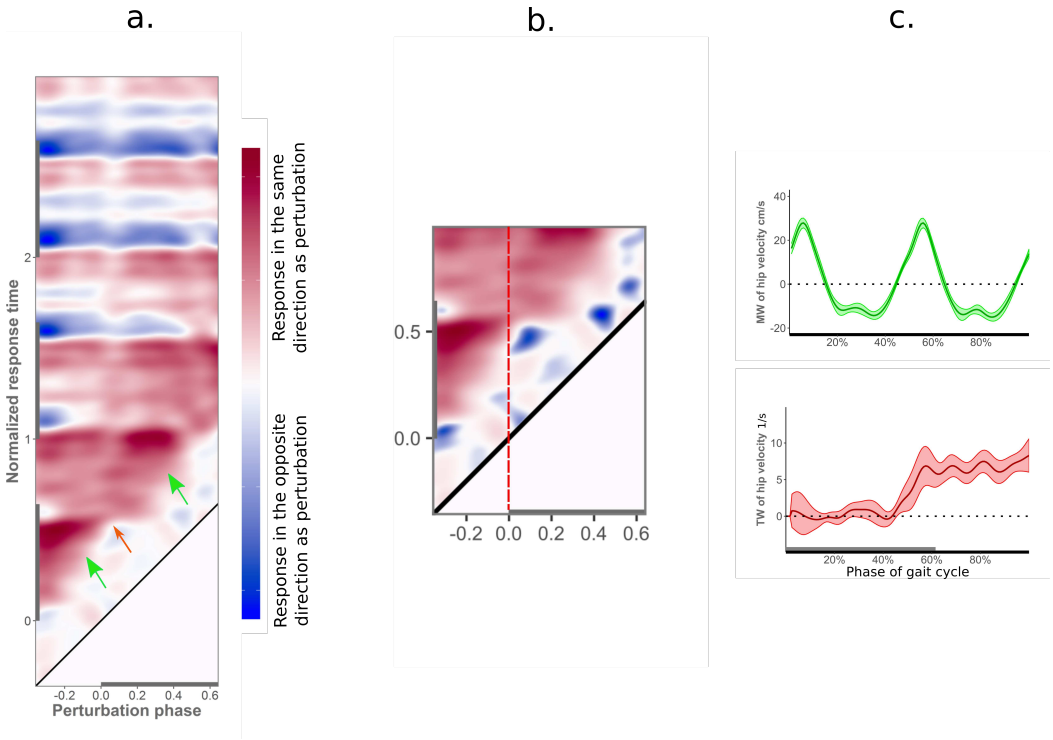

Figure 3.10. **a.** φIRFs for hip velocity showing responses for three cycles following perturbation. The grey bars on axes mark the stance phase. The green arrows show the major regions of increase in speed. The orange arrow marks the start of a gradual change in speed. **b.** Responses from the first cycle highlighted. Each slice of the 2D plot is an IRF for a specific phase. The red dashed line marks the response to perturbation from heel-strike. **c.** Top is the MW averaged across all cycles and bottom is the slice highlighted in part **b**).

speed by looking at antero-posterior movement of the hip markers. The velocity of both hips averaged together gives an estimate of the center line of the body close to the center of mass. Similar to the approach used for EMGs we can calculate φIRFs for the hip velocity. Figure 3.10a shows the φIRF for the hip midpoint AP velocity. The green arrows on the graph mark two instances of major increases in speed. These two regions are half a cycle apart due to the symmetry of bipedal gait. The increase in speed in these regions is gradual and starts well in advance of the peak of activity. The orange arrow marks the approximate start of the

change in velocity. Figure 3.10b shows a zoomed in view of the first cycle from part a. To better understand the changes in speed we choose to look at the effect of perturbation at heel-strike. This slice is marked by the red dashed line in the figure. Figure 3.10c shows the MW pattern for the hip velocity averaged over all cycles in comparison to the TW from the slice highlighted in part b. As mentioned before the TW happens on top of MW meaning that the total response is the TW plus the MW. TW for the hip velocity clearly shows that increase in speed as a result of perturbation starts at about 50% of the cycle which is before the start of push-off phase. It is noteworthy to mention that this transient change of speed in response to a perturbation delivered around the heel-strike happens after the observed decreases in plantarflexors activities in response to the same perturbation (Figure 3.7).

In addition to quantifying the effect of perturbation on control of speed as part of the goal of this study, we also aimed to compare the changes in mean waveforms between unperturbed and perturbed conditions. To demonstrate that averaging across all gait cycles in the time domain (i.e., constructing MW profiles) shows similar patterns in both unperturbed and perturbed walking, we calculated the area under MW profiles during stance and compared them between unperturbed and perturbed conditions using t-tests. For plantarflexors, student t-tests showed no significant difference between MW of unperturbed and perturbed walking conditions. The p-values for SOL, GASl, and GASm were 0.6, 0.67 and 0.86 respectively.

3.4 Discussion

Revisiting the first goal of this study, we can conclude that there are similarities between changes in muscle activations that lead to a transient change in speed and changes in the mean periodic pattern of muscle activations with a change in the speed of steady-state walking. The majority of muscles show activations in the same part of the gait cycle which matches the observations from previous studies. There are, however, some differences between the two conditions for plantarflexor muscles. The φIRFs clearly show periods of decrease in the activity of plantarflexors (Figure 3.9) that presumably contribute to the change in speed (Figure 3.10). Although the mechanism for this contribution is not well understood, a few studies in recent years have proposed that desired changes in speed could be achieved not only by increasing the propulsive impulse from plantarflexors at the time of push off but also through a decrease in the braking impulse in early stance [34,118]. However, none of these studies have measured muscle activities and the conjectures made have been based on calculations of heel-strike and push-off impulses and joint moments through inverse dynamics using kinematic and ground reaction forces data. Without looking at muscle activation patterns it is not possible to make conclusive statements about the contribution of each muscle to control of speed. Here for the first time through comparisons of transient responses to changes between steady-state conditions, we showed that plantarflexors may contribute to changes in speed during during early to mid-stance part of the gait cycle and this modulation is missing from control of speed in steady-state walking.

Another goal of this study was to compare functional role of muscles in control of walking during transient responses to their role during changes applied in steady-state conditions. The small changes in the mean waveforms showed agreement with previously observed increases in activations for different groups of muscles during larger increases in speed [119, 120] and transient responses were similar to those previously described [19]. The dorsiflexor, plantarflexors, knee and hip extensors, knee and hip flexors and trunk muscles all provide support and progression during the same phases of the cycle as steady-state walking. The results show that the response of the system to the perturbation from early stance is decreasing the activity of plantarflexors in mid-stance and increasing it during late stance in order to increase the speed and counteract the effect of perturbation [19]. In this study we showed that this relationship did not exist in steady-state walking. This information could be used as a guideline for future studies to better explore the causal relationship between modulations of muscle activations and changes in speed.

3.4.1 Limitations and future work

In this study, we analyzed the system using the local limit cycle (LLC) approximation. This means that we assume the responses to movements of the visual scene toward the subjects are the same in magnitude but opposite in sign as the reactions to movements away from them. For small perturbations this assumption is valid. However, for large perturbations, it has been shown that subjects have larger responses to movements toward them compared to movements away from

them [121]. So it is not clear how the results of our study would change for larger perturbations.

Another limitation of this study was in the measurement of muscle activations. We used surface EMG which means that the recordings were not at the level of motor units. Intramuscular recordings may result in more details about subtle changes in transient responses. We also assumed symmetry exists and only recorded from the right side of the body. Future studies can collect from more muscles involved in the control of walking (e.g., sartorius muscle) and also collect data from both sides to have a complete assessment of muscle activations.

We did not test for significance of changes in transient responses between the two speeds used in this experiment. Although the goal of our study was to compare qualitative features of transient activities to changes in MW from steady-state walking and even though the visual inspection of results (Figure 3.5) showed similar patterns at both speeds, it is not clear if the change in speed had any effect on the amplitude and phase of responses since no quantitative comparisons or statistical tests were applied to evaluate the effect of average speed (i.e., treadmill speed) on the responses. The proposed study in chapter 4 will address this question.

The nature of comparisons between transient and steady-state behavior may also be subject to investigation. Here, we compared transient changes to changes between two different speeds of steady-state walking. However, these changes are derived using signals from walking at two different speeds that happen in two different trials. One can argue that humans change their steady-state speeds by accelerating or decelerating thereby increasing or decreasing the speed gradually and continu-

ously from one level to another. It is not clear if changing speed in this fashion results in similar differences we observed in our data. Furthermore, it is not known if the transient changes that happen during the transition between two steady-state speeds are similar to transient changes in response to perturbations or if the nervous system employs a different control strategy for increasing speed between the two conditions. These questions are open to investigation for future studies.

4

Visual perturbations and average speed of walking

For such a model there is no need to ask the question "Is the model true?". If "truth" is to be the "whole truth" the answer must be "No". The only question of interest is "Is the model illuminating and useful?".

George E. P. Box, statistician

4.1 Introduction

The goal of the previous chapter was to compare the transient changes in muscle activations that cause transient changes in walking speed to the small difference in mean activation waveforms from steady-state walking at two different treadmill speeds. To achieve this goal, we chose two treadmill speeds close to each other. As a result, our study did not address how treadmill speed affects transient changes in muscle activations in response to visual perturbations. In this chapter we focus on this question. Similar to the approach used before, we invoke transient responses in subjects by perturbing their gait visually while walking on the treadmill. However, in this study there will be substantial differences in treadmill speed across conditions. The pattern of transient responses will be revealed by using the system identification and signal processing techniques explained in Chapter 3.

4.1.1 Research question

This study seeks to quantify how the transient responses to visual-scene motion depend on treadmill speed. We hypothesize qualitatively similar patterns in transient responses among different speeds. As was discussed in Chapter 2, perturbations of the visual scene have shown greater effects on control of locomotion at lower speeds and it has been suggested that this effect might be due to the involvement of highly automated spinal locomotor programs at higher speeds [50]. Additionally, some studies in animals have provided evidence for existence of separate neural circuits controlling gait at different speeds [122, 123]. Based on these

ideas that suggest differences in control at different speeds, it is possible that we see larger effects on transient responses at lower treadmill speeds even though the patterns might be qualitatively similar as we hypothesize.

4.1.2 Specific aim

To determine responses in muscle activations due to the motion of the visual scene during walking at different treadmill speeds. Hypothesis: There will be changes in transient responses consistent with the amplitude of responses increasing with increasing speed. We expect to see larger increases in amplitudes at lower treadmill speeds.

4.2 Methods

The experimental protocol was approved by the Institutional Review Board (IRB) at the University of Maryland. The procedures for data collection including the apparatus used and the design of perturbation signals are all similar to the previous study and are described in details in section 3.2.

4.2.1 Data collection

Eighteen healthy subjects (13 females) between the ages of 18 and 30 (mean: 20.9) with no neurological disorder participated in this study. The testing procedure was explained to the participants and their written consent was obtained prior to experiments. Subjects walked on the treadmill in the virtual reality room. Before

trials start subjects walked on the treadmill in front of the screen to familiarize themselves with the experiment setup. The experiment setup was similar to the one used in the previous study. However, instead of two close treadmill speeds, three speeds from a wider range was used here. Subjects walked for eighteen trials at speeds of $0.94, 1.16$, and 1.39 m/s ($2.1, 2.6$, and 3.1 miles/h). This range encompassed an increase of about 48% in speed. There were six combinations for order of speeds with each combination having three subjects assigned to it so that the effect of speeds order on the outcome was minimized. At each speed, the first and last trials captured the unperturbed walking and the other four trials captured visually-perturbed walking. The total time of the experiment was approximately three hours. Subjects were allowed to take breaks between trials whenever they needed. Kinematic and EMG data were recorded as described in Chapter 3.

4.2.2 Analysis

The HTF method was used to analyze the data in frequency domain and the results were converted to time domain to form φIRFs. Slices of φIRFs show the transient changes in muscle activations caused by a perturbation at specific phase of the gait cycle. The transient changes were compared across different treadmill speeds to identify significant differences. A qualitative comparison was made between transient changes and the changes in the mean waveform at different speeds.

To examine the significance of the relationship between speed and EMG activity over the entire gait cycle, 95% confidence intervals were constructed for the data.

Areas where the confidence intervals included zero indicated insignificant changes. To control the family wise error, a modified version of the tmax method [112] was used. In this method we used the maximum absolute value of the EMG signal instead of the maximum absolute t-value. The method used bootstrapping (100000 bootstrap samples) to calculate p-values defined based on the maximum value of φIRFs. This determined if the φIRF that was averaged across all subjects was significantly different than zero or not. If the averaged φIRF for a muscle is significantly different than zero then the slices of the φIRFs for that muscle can be used for analysis.

4.3 Results

Transient responses and the mean waveforms at all speeds for lower leg and upper leg muscles are depicted in Figure 4.1 and Figure 4.2. Transient responses are responses to a forward impulse in visual scene velocity (a forward step in visual scene position). As a reminder, similar to Chapter 2, transient responses were recorded from fourteen muscles: TA, SOL, GASl, GASm, RF, VASl, VASm, BF, SEMT, TFL, GLmed, GLmax, ESL, and EST. Although we observed statistically significant responses in most muscles, a few muscles did not show significant responses at some speeds. RF did not show significant changes at 1.39 m/s (p-value>0.05). VASl changes were not significant at 0.94 and 1.16 m/s. TFL and ESL did not have significant responses at 0.94 and 1.16 m/s and GLmed and GLmax responses were not significant at any speed. As Figure 4.1a shows, forward movement of the visual

scene during the swing caused an increase in the activity of TA in early stance. Concurrently, VASm showed an increased activity in early stance in response to visual scene moving forward during the swing (Figure 4.2a). SOL activity increased close to push-off in response to visual scene moving forward in mid-stance (Figure 4.1b). SEMT increased its activity in late swing in response to visual scene moving forward during the swing (Figure 4.2b).

Figure 4.3 and Figure 4.4 show maximum transient responses (vertical slices of φIRFs through the largest increase in activity) at the three speeds for lower leg and upper leg muscles respectively. All muscles show qualitatively similar patterns of changes across speeds. TA, VASm, and SEMT did not show any significant effect of treadmill speed on the pattern of transient responses. Comparison of SOL activity between 0.94 and 1.16 m/s shows a direct increase with speed in late stance (Figure 4.3) similar to the pattern for unperturbed walking. GASl shows an increase in the activity in late stance from 0.94 to 1.16 m/s and GASm activity shows a small increase during early stance from 0.94 to 1.16 m/s.

4.4 Discussion

Majority of muscles showed significant transient responses at different speeds. An approximately linear scaling effect of treadmill speed on the amplitude of transient responses was observed in plantarflexors. The increase in activity of SOL and GASl for lower speeds was compatible to increases in mean waveform reported in the literature. The amplitude of GASm did not show a strong effect of scaling from

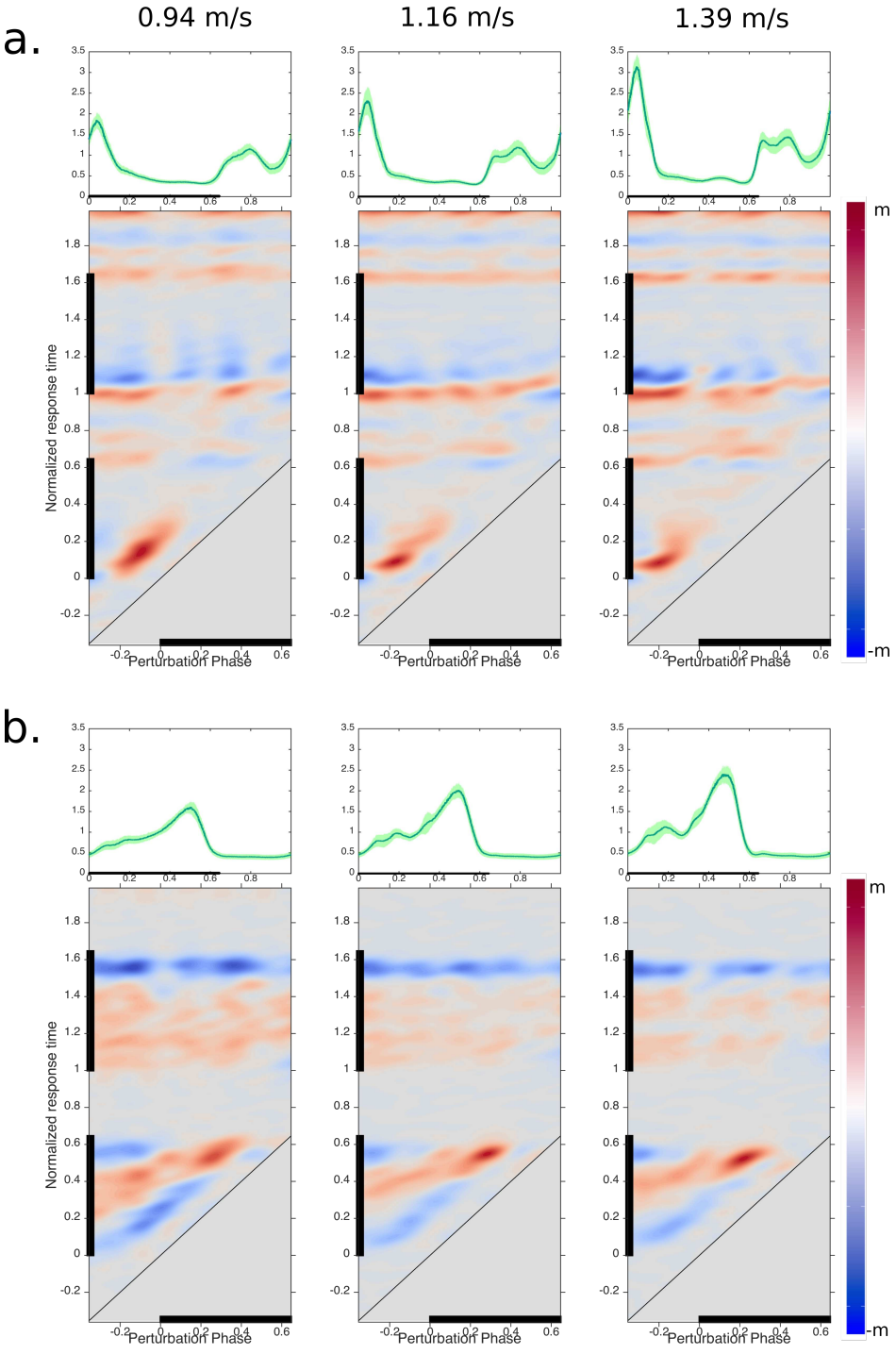

Figure 4.1. **a.** φIRFs for TA showing responses for two cycles following perturbations at the three speeds of 0.94, 1.16, and 1.39 m/s (2.1, 2.6, and 3.1 miles/h). The black bars on axes mark the stance phase. The top plots in green show the mean waveforms. m = 0.07 cm^{-1}. **b.** φIRFs for SOL showing responses for two cycles following perturbations at the three speeds. m = 0.08 cm^{-1}.

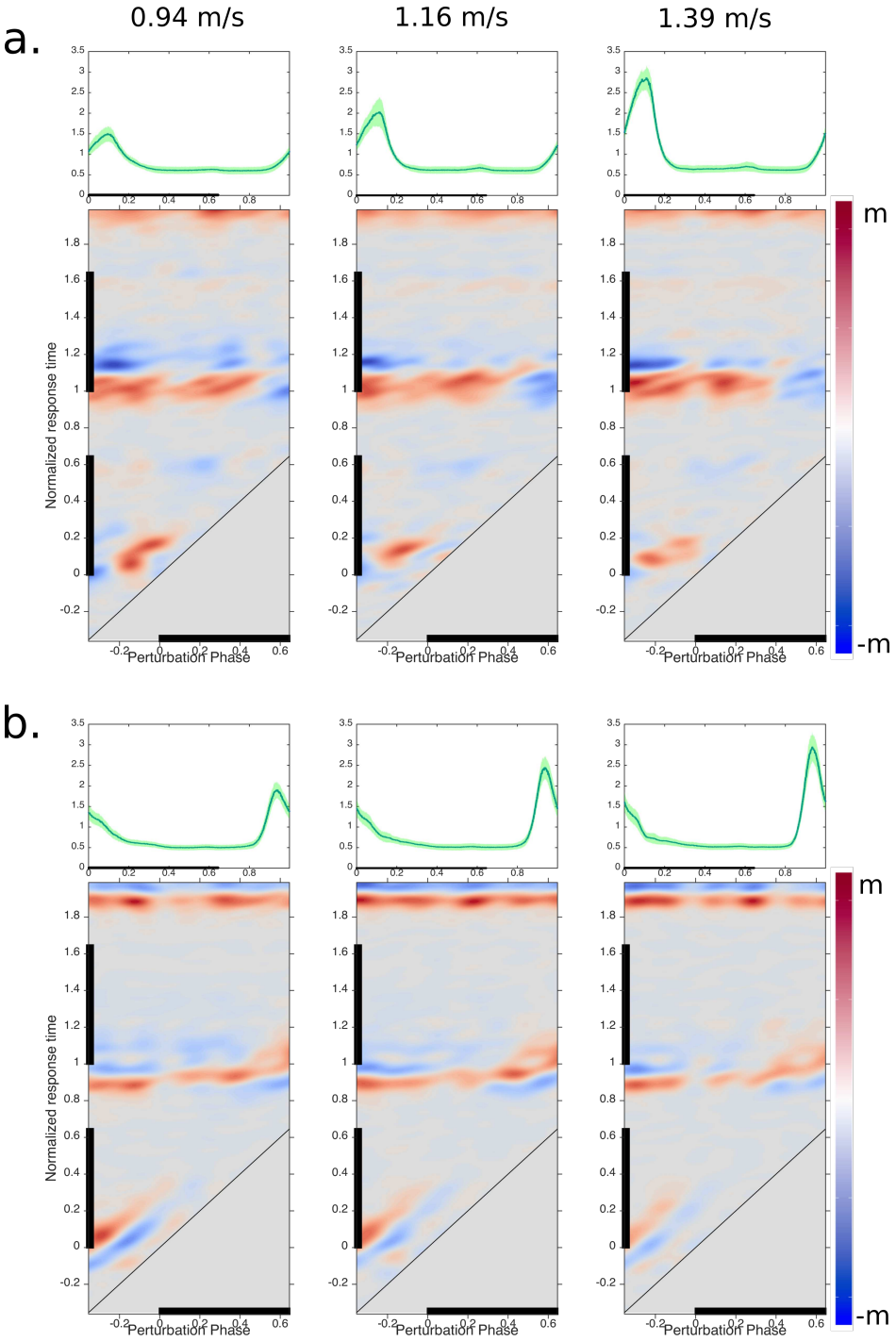

Figure 4.2. **a.** φIRFs for VASm showing responses for two cycles following perturbations at the three speeds of 0.94, 1.16, and 1.39 m/s (2.1, 2.6, and 3.1 miles/h). The black bars on axes mark the stance phase. The top plots in green show the mean waveforms. m = 0.04 cm^{-1}. **b.** φIRFs for SEMT showing responses for two cycles following perturbations at the three speeds. m = 0.07 cm^{-1}.

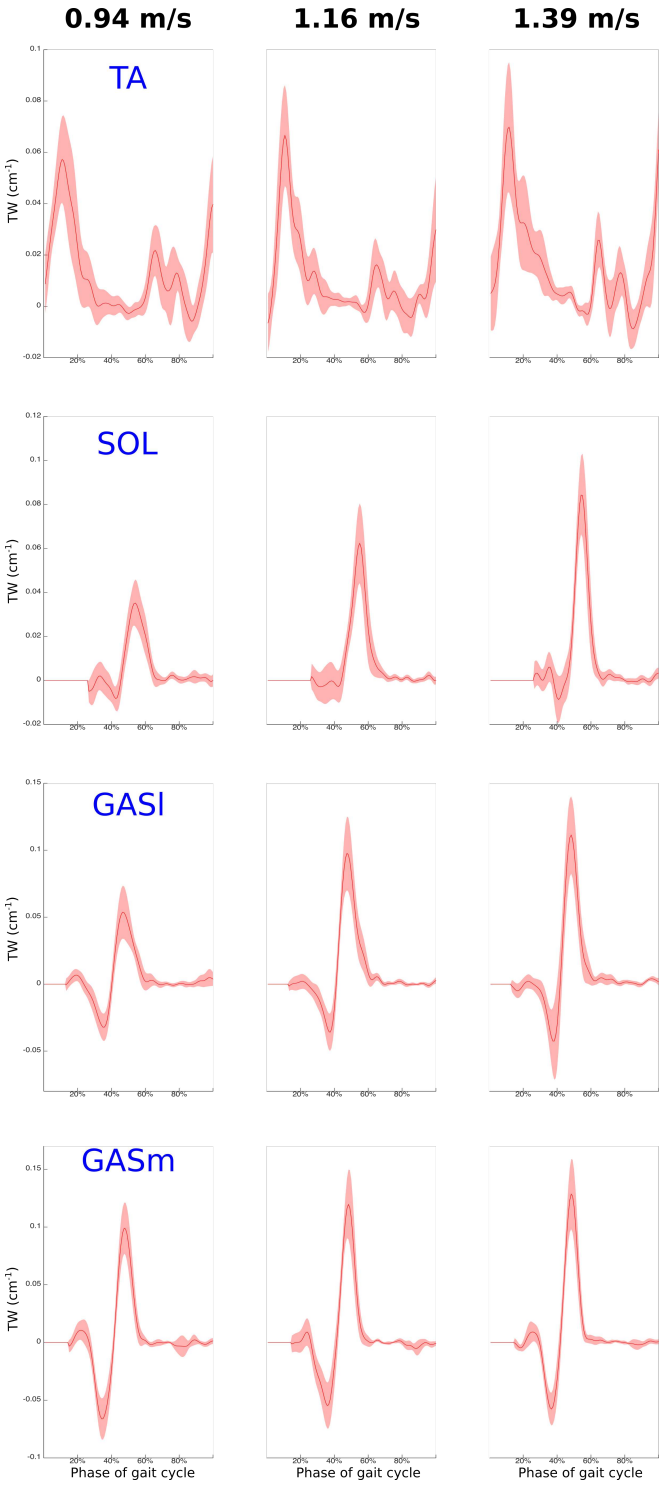

Figure 4.3. Transient waveforms (slices of φIRFs) for TA, SOL, GASl, and GASm at three speeds of 0.94, 1.16, and 1.39 m/s (2.1, 2.6, and 3.1 miles/h).

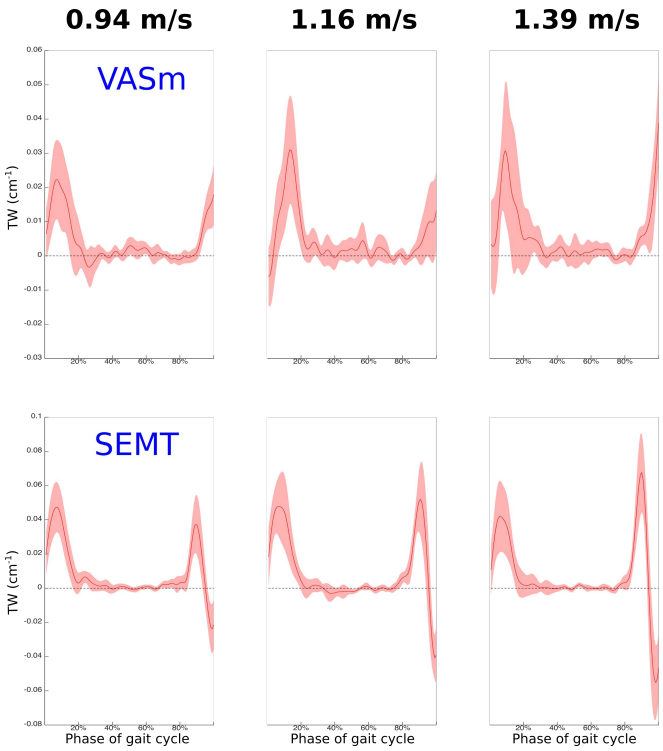

Figure 4.4. Transient waveforms (slices of φIRFs) for VASm and SEMT at three speeds of 0.94, 1.16, and 1.39 m/s (2.1, 2.6, and 3.1 miles/h).

the treadmill speed. From 1.16 m/s to 1.39 m/s which is an interval that contains the speeds we used in Chapter 3, muscles did not show significant effects of treadmill speed on transient responses. This confirms that our assumption of similarities of responses was reasonable.

Even though we recruited 18 subjects in our study, it is possible that the sample size has not been enough to detect some of the smaller effects of treadmill speed on amplitude modulations. The timing of the peak did not show substantial changes across speeds. These modulations are qualitatively similar to the observed patterns from unperturbed walking. This outcome provides a measure of dependency of transient responses on walking speed and a comparison to the effect of speed on modulation of muscle activations in steady-state walking. Further comparisons and

larger sample sizes are needed to draw conclusions for all muscles.

In steady-state walking, some studies have argued in favor of an approximately linear relationship between speed and muscle activity mainly based on the idea that similar muscle synergies (i.e., motor modules) control walking and thus the effect of speed is reduced to linear scaling of weights of synergies [93, 94, 124]. However, this may not be true for transient responses to perturbations. As we discussed in Chapter 2 it has been reported that visual perturbations have greater effects on control of walking at lower speeds [50]. Some animal studies have also suggested that locomotion at different speeds might be controlled by different neural circuits in the brainstem [122, 123]. In this study, we did not find significant effects of speed on transient responses for some muscles. If differences in control exist at different speeds it is possible that transient responses get affected differently at different speeds. Further investigation is required to test this idea.

5

Mechanical perturbations of speed

With four parameters I can fit an elephant, and with five I can make him wiggle his trunk.

John von Neumann

the father of game theory

5.1 Introduction

In the previous chapters, we discussed the relationship between muscle activity and speed of walking. We used visual perturbations to elicit responses in subjects to modulate their muscle activations in order to control their speed. Also, we used the average speed (i.e., treadmill speed) as an independent variable and we examined its effects on transient changes in muscle activity during control of speed. As discussed in the first chapter, the use of visual perturbations requires the short latency method of inference to make assumptions about how the nervous system interprets the movement of the visual scene, whereas for mechanical perturbations this limitation does not exist. Application of mechanical perturbations allows us to quantify the input to (i.e., kinematics) and the output from (i.e., EMG) the neuro-feedback and estimate the controller dynamics [18, 19, 21]. As mentioned before the non-parametric system identification approach used here cannot fully identify the system since we are not independently perturbing all degrees of freedom. However, our goal in this series of studies was to apply sensory and mechanical perturbations to provide enough insight into the system to allow us to predict its behavior in most conditions. To this end, we propose a study in this chapter to explore transient changes in muscle activity in response to mechanical perturbations of the treadmill belt.

5.1.1 Research question

In Chapter 3 (Figure 3.7 and Figure 3.9) we showed that during transient responses, the activity of plantarflexors decreases early in the stance around the same time that a decrease in braking impulse has been reported in recent studies from the literature [33, 34]. This may suggest a role for plantarflexors in control of speed different than the traditional view of their contribution at push off. We have also seen an increase in the activity of TA around heel-strike in response to perturbations during the swing. The role of these responses in control of walking is not well understood yet. Especially it is not clear if the same changes in muscle activations are elicited in response to mechanical perturbations of the treadmill, a form of perturbation that has been applied in several recent studies [100–102]. The purpose of this study is to further explore transient changes in muscle activations in response to continuous broadband perturbations of the treadmill belt and to infer from the evoked transient responses how walking would respond to velocity impulses. Additionally, the functional role of responses in control of walking will be analyzed.

5.1.2 Specific aims

Aim #1: To characterize properties of neurofeedback using a system identification approach. The relationship between changes in kinematics due to mechanical perturbations and modulations of muscle activations (reflected in EMG recordings) as the response of the neural controller to said changes will provide knowledge about neurofeedback. We hypothesize that the nervous system will increase the activity of

plantarflexors at push off in response to perturbations early during the stance. We may observe some decrease in the activity before mid-stance similar to responses to visual perturbations but this behavior as well as responses of other muscles are less explored and their identification requires further investigation.

Aim #2: To compare and contrast transient responses to mechanical perturbations to those observed in response to visual perturbations in previous studies. We expect to observe some similarities between the transient changes in activations between the two different types of perturbation. Comparing responses to visual perturbations with responses to mechanical perturbations, it is easier to make inferences about properties of neurofeedback looking at responses to mechanical perturbations.

5.2 Methods

This section describes the experimental design. Subject recruitment, apparatus used, design of perturbation signals, instructed protocol, and the analysis methods are discussed.

5.2.1 Subjects

The experimental protocol was approved by the Institutional Review Board (IRB) at the Cleveland State University. Fifteen subjects (6 females) between the ages of 18 and 33 (mean 25.3) with no neurological disorder volunteered to participate in this study. Each subject was briefed on the procedures and their written informed consent was obtained prior to the experiment.

5.2.2 Apparatus

An instrumented split-belt treadmill (Forcelink, Culemborg, Netherlands) was used to apply antero-posterior belt perturbations. Force plates under the belts recorded the ground reaction forces. Two XSENS accelerometers (Enschede, Netherlands) were attached to the treadmill to capture its dynamics. Kinematics was captured using a 10 Osprey camera system operated through Cortex motion capture software (Motion Analysis, Santa Rosa, CA, USA). Twenty reflective markers were attached to the body on different anatomical landmarks including lateral malleolus (ankle), lateral femoral condyle (knee), greater trochanter (hip), sacrum and acromion (shoulder). Three markers were attached to the shoes where the posterior calcaneus (heel), the big toe, and the 5th metatarsal were located. Five markers were attached to the treadmill to capture its movements. D-Flow software (version 3.20.1) was used to send perturbation commands to the treadmill. Since a blank screen can result in subjects adapting a more cautious gait while walking on the treadmill [58], a visual display system (Motek Medical, Amsterdam, Netherlands) was used to project a natural path in front of the treadmill. However, the visual scene was kept static to avoid any interference between the effects of the optic flow and the effects of mechanical perturbations on the perception of speed. A wireless 16 channel TRIGNO system (DELSYS, USA) was used to capture EMG signals. Fourteen muscles on the right side of the body were recorded: tibialis anterior (TA), soleus (SOL), gastrocnemius lateralis (GASl), gastrocnemius medialis (GASm), rectus femoris (RF), vastus lateralis (VASl), vastus medialis (VASm), bicep femoris

(BF), semitendinosus (SEMT), tensor fascia latae (TFL), gluteus medius (GLmed), gluteus maximus (GLmax), erector spinae lumbar (ESL), erector spinae thoracic (EST). The belly of each muscle was located according to SENIAM guidelines [104] and the recording site was cleanly shaved and abraded with alcohol swabs. Data was recorded at the sampling rate of 1000 Hz. A harness was used at all times during walking trials to ensure the safety of subjects.

5.2.3 Perturbation

Perturbations with two different amplitudes were used in the experiment. The higher amplitude perturbation was designed to be similar in amplitude to the one previously used by Moore et al. [102]. We used velocity signals as our inputs. To create the higher amplitude input, white noise with a spectral density of 0.002 m^2/Hz was low-pass filtered at cutoff frequency of 5 Hz using a second-order Butterworth filter. This frequency range is similar to the visual perturbations used in previous chapters which showed significant responses from the nervous system in modulation of transient muscle activations. To observe the local limit cycle behavior of the system, perturbation signals have to be sufficiently weak. Based on this requirement a lower amplitude signal was designed similar to the higher amplitude one but with half the power. We differentiated each velocity signal to check for acceleration limits. If a seed violated the maximum acceleration constraint of 15 m/s^2 it was discarded. Less than 5% of the seeds met the exclusion criterion. Perturbation signals were piloted before the start of subject recruitment. The higher amplitude perturbation

was noticeable although not large enough to create stumbling or any large instability. During the data collection, none of the subjects found the perturbations to be large.

The choice of velocity as the input was based on its transient effects. Since in our computational approach we are inferring the response to an impulse in the input we are assuming that subjects recover from the perturbation, which means that they show a transient change in the response. An impulse in velocity has this characteristic. But an impulse in acceleration, for instance, is equivalent to a step in velocity, which means that subjects' velocities do not have to recover from the change in the input. An impulse in position can be another choice. A foot in contact with the belt will follow the position impulse. However, since the effect on the belt is very brief (it moves forward and then immediately moves back), there may not be a need for the nervous system to respond to the perturbation.

5.2.4 Protocol

Subjects wore athletic shorts and running shoes. EMG sensors and reflective markers were attached to the body according to the procedures described in the Apparatus section. Subjects walked on the treadmill during ten trials and were instructed to look at the static visual scene in front of them and to try to stay close to the treadmill midline and not drift to the sides. Each trial was 250 seconds and the first and last trials captured unperturbed walking. In the remaining trials, perturbations were applied to the belt in anteroposterior direction. Four trials used

the lower amplitude signals and four applied the higher amplitude with the order of all being randomized. After each trial, subjects were asked about the difficulty of the task and they were allowed to take a break if needed. All markers and EMG signals were monitored in Cortex during each trial to make sure every information was captured.

For all trials, the average speed of the treadmill was set to 1.3 m/s. A recent study [125] which has elaborately reviewed hundreds of publications on the preferred speed of walking has reported this value as the best estimate of average walking speed in most environments. This value is also within the range used in previous chapters and suggested by several studies as the choice for preferred or comfortable speed [105–107].

5.2.5 Analysis

The EMG signals were high-pass filtered at 20 Hz using a fourth order Butterworth filter to remove movement artifacts then rectified. Kinematic and EMG signals were expressed as functions of estimated phase [19]. The gait cycle starts at the phase of zero (i.e., heel-strike) and ends at 100% (i.e., next heel-strike). The data was then averaged over all cycles and then over all trials to obtain one mean waveform for each subject. The trials of each condition for each subject were then normalized to the mean waveform obtained for that subject. The gait cycles were visually inspected to exclude any outliers due to stumbling or other possible irregularities. The anteroposterior direction towards the front of the treadmill was

considered as positive for marker trajectories. For the leg angle (i.e., the angle between the hip and the ankle), the forward movement (i.e., ankle in front of the hip) was defined as positive. For the ankle, dorsiflexion was considered positive. The knee and hip angles were defined positive in flexion.

To estimate responses, the speed signals commanded to the treadmill were used as the input signals, since unlike the measured signals the commanded ones were not affected by the subjects' movements on the treadmill. The measured signals are obtained from a closed loop in which the walking of the subject on the belt affects the measured belt speed. We showed that this effect was reflected in the speed of the belt averaged over all cycles. Figure 5.1 shows the mean waveform of the measured speed and the φIRF of the measured speed as a function of the commanded speed. While we expected the average speed to be 1.3 m/s, the figure shows deviations ($\sim 1\%$) in the belt speed as a result of the subject walking on the belt.

Since the low-pass filter we used to create perturbation signals did not have a sharp cutoff at 5 Hz, the perturbation signals had sufficient power up to about 8 Hz. This allow us to use 8 as our maximum normalized frequency for the input. Using the same approach applied in previous chapters and elaborated in [19], the φIRFs between mechanical perturbation as the input and kinematics as the output and between mechanical perturbation as the input and EMG as the output were calculated. The φIRF has two components: one is the transient component of the response that fades away one or two cycles after the onset of perturbation and the other component is due to the phase resetting. The combination of both of these components provides information about the system in a contour plot that depicts

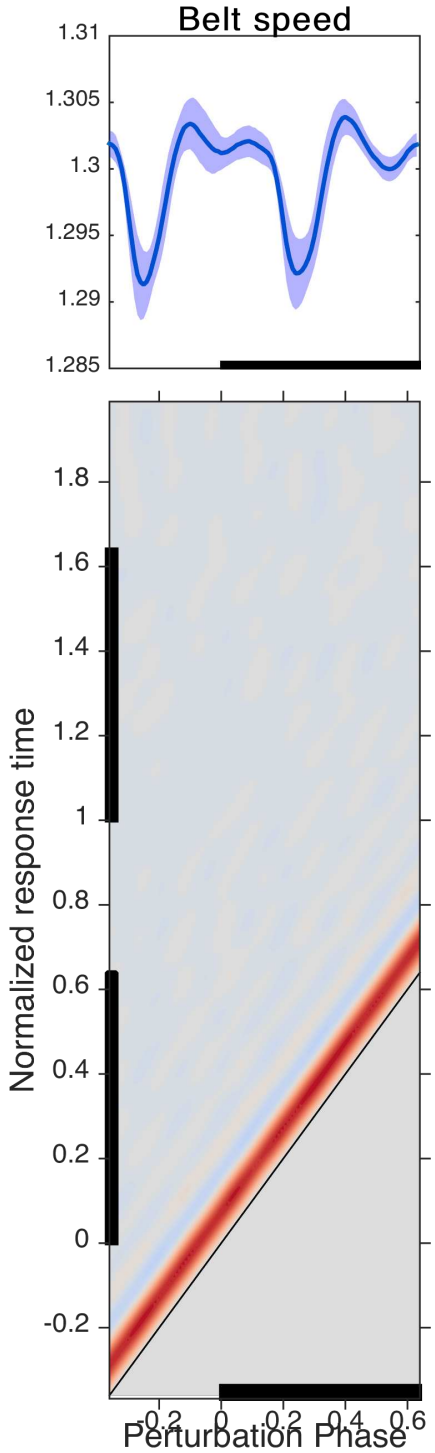

Figure 5.1. **top.** Mean waveform of the measured belt speed. As we can see the speed oscillates around 1.3 m/s **bottom.** φIRF of the belt speed with commanded speed as the input and measured speed as the output.

φIRF as a function of the phase at which the perturbation is delivered (horizontal axis) and the phase at which the response is observed (vertical axis). We will refer to the latter as "normalized response time" to distinguish it from phase as a dependent variable. The φIRFs are calculated for all muscles and major kinematic variables and will be compared in the next section to the results from visual perturbations.

Statistics. The t-based 95% confidence intervals were built for all kinematic variables and EMGs [115]. Since for each response variable the phi-IRF describes responses for a range of perturbation phases and normalized response times, the tmax method [112] was used to control the family wise error. The method used bootstrapping (100000 bootstrap samples) to calculate p-values defined based on the maximum value of φIRFs (the entire φIRF not just one slice). This determined if the φIRF that was averaged across all subjects was significantly different than zero or not. If the averaged φIRF for a muscle is significantly different than zero then the slices of the φIRFs for that muscle can be used for analysis otherwise responses for that muscle are not significant.

For both steady-state and transient profiles 95% confidence intervals were constructed. In the areas where confidence intervals include zero, the steady-state or transient activity is not significantly different than zero. To adjust the p-values and control the family wise error, the tmax method [112] was used for kinematic data. The method used bootstrapping (100000 bootstrap samples) to calculate p-values defined based on the maximum value of φIRFs. This determined if the φIRF that was averaged across all subjects was significantly different than zero or not. If the averaged φIRF for a muscle is significantly different than zero then the slices of the

φIRFs for that muscle can be used for analysis. A modified version of the tmax method was used for EMG data. In this method we used the maximum absolute value of the EMG signal instead of the maximum absolute t-value.

5.3 Results

The φIRF of the heel velocity and the leg, ankle, knee, and hip angles were significant for higher perturbation. At lower perturbation all but the heel velocity φIRF were significant.

Kinematic responses to single-support perturbation. The responses of the joint angles to the perturbation are depicted in Figure 5.2 for both ipsilateral (5.2b) and contralateral (5.2c) legs. The perturbation was delivered at 24% of the gait cycle during which the ipsilateral leg is close to mid stance and the contralateral leg is in the early swing. The top row (5.2a) shows the mean waveform for each kinematic variable averaged over all gait cycles.

As explained in previous chapters, responses are slices of φIRFs calculated using the HTF approach. In other words, each plot is a slice showing the transient changes in the the output variable as a function of the perturbation (i.e., the input) applied at a specific phase of the gait cycle. The mean waveforms were subtracted from the signals before the calculation of transient responses. This means that the value for each variable at each point in the cycle is the sum of the mean waveform value (from Figure 5.2a) and the transient response (from Figure 5.2b or Figure 5.2c). Since the sign convention assumed a positive direction for the antero-

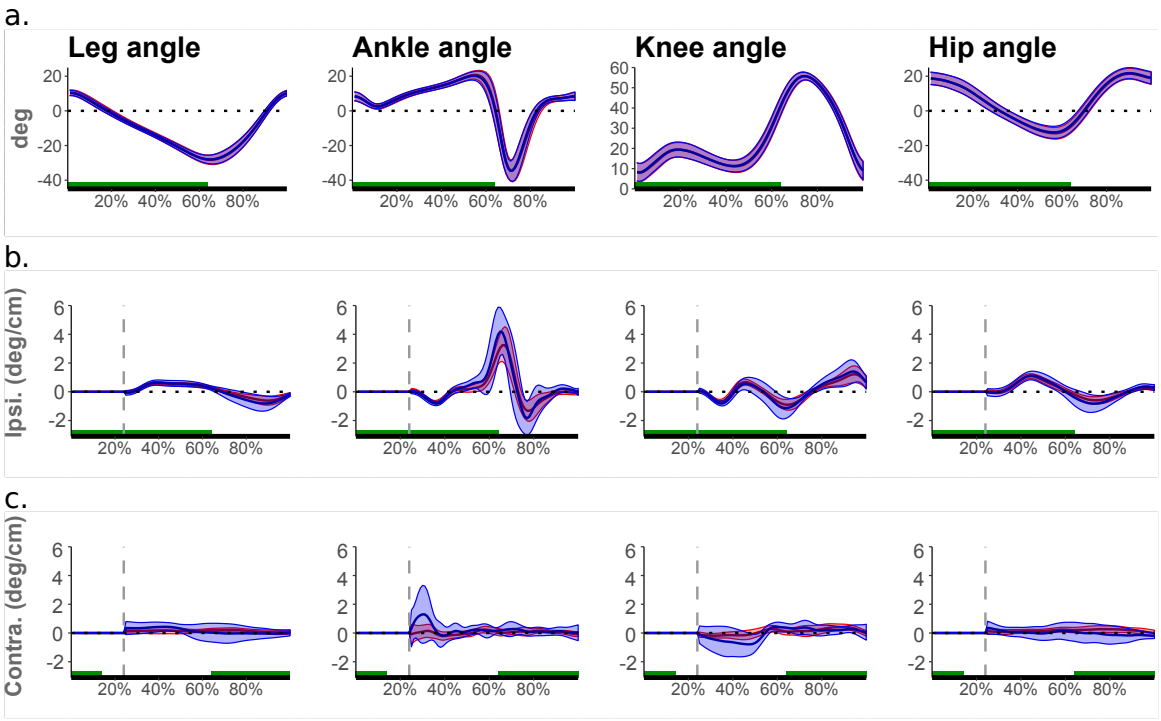

Figure 5.2. *Kinematic responses to single-support perturbation.* **a.** Mean waveforms for the leg angle and the ankle, knee and hip joint angles for the higher (red) and the lower (blue) perturbations. **b.** Kinematic responses of the ipsilateral leg. The grey dashed line marks the onset of perturbation and the green bar highlights the stance phase. **c.** Kinematic responses of the contralateral leg.

posterior movements toward the front of the treadmill, the transient changes shown in the figure are responses to a forward impulse in tread velocity which causes a plantarflexion during mid stance. Since we are assuming a local limit cycle approximation, responses to a backward impulse are assumed to be equal in size and opposite in sign to those presented in the figure. All the transient changes in this section are presented as responses to a forward impulse in velocity.

Unlike visual perturbations, mechanical perturbations immediately affect kinematics of the limbs. As Figure 5.2b shows, changes are observed in all angles of the ipsilateral leg immediately after the onset of perturbation. Since the ipsilateral leg is

in mid stance with the foot sole being in full contact with the belt, the perturbation introduces a plantarflexion, which causes the leg to move forward (angle increase), the ankle to plantarflex (angle decrease), the knee to extend (angle decrease) and the hip to flex (angle increase). On the other hand, the perturbation does not result in any statistically significant kinematic changes in the contralateral leg, which is in the early swing. In this study since we used small perturbations, when a leg is not in touch with the belt it may not show statistically significant changes in kinematics and EMG.

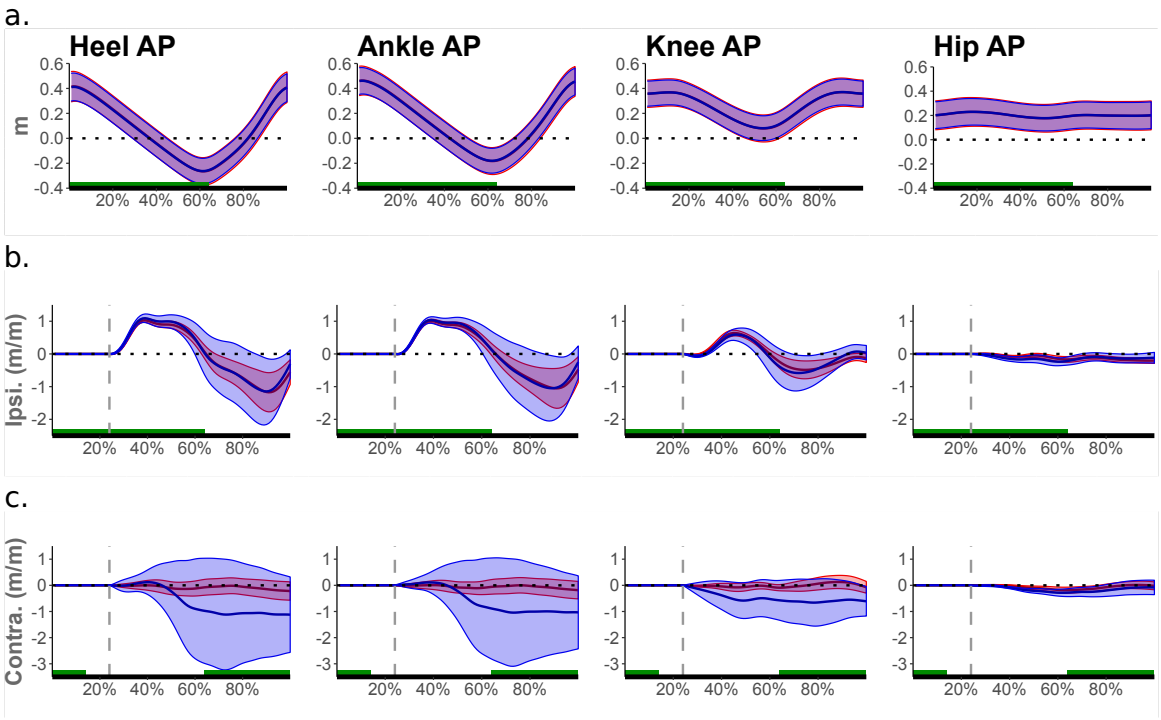

Figure 5.3. *Kinematic responses to single-support perturbation.* **a.** Mean waveforms for the heel, ankle, knee and hip markers AP trajectories for the higher (red) and the lower (blue) perturbations. **b.** Kinematic responses of the ipsilateral leg. The grey dashed line marks the onset of perturbation and the green bar highlights the stance phase. **c.** Kinematic responses of the contralateral leg.

Due to the local effects of mechanical perturbations, the changes in kinematics

of markers can also provide valuable information about responses. Figure 5.3 shows transient changes in the AP trajectories of the heel, ankle, knee and hip markers. Of all the markers on the body, the heel is the foot markers are the ones we expect to have the closest trajectories to the movement of the belt. Since the perturbation is an impulse in the velocity it should create an approximate step in the position of the heel. This can be verified in Figure 5.3b which shows following its initial rise the heel AP coordinate stays close to the set value of one during the stance until around the heel-off after which the foot is not in full contact with the belt. The ankle marker which is close to the heel also shows a similar pattern. The knee moves forward in response to the perturbation but the hip position does not show any significant changes. None of the markers on the contralateral leg (Figure 5.3c) show significant responses. This is in agreement with the lack of changes in joint angles from Figure 5.2c.

Figure 5.4 shows φIRF plots for four lower leg muscles. They all show responses to perturbations delivered at different phases and the mean waveforms (on top) match the patterns reported in literature and discussed in previous chapters. For the larger perturbation, the responses described by φIRFs were significant for all muscles but TFL, GLmax and GLmed (p-value$<$0.05). φIRFs were significant for all muscles except BF, SEMT, ESL, TFL, GLmax and GLmed for the smaller perturbation.

EMG responses to single-support perturbation. As discussed in Chapter 1, kinematic changes are inputs to the neural controller. These changes will require the neurofeedback to modulate muscle activations in order to correct the kinematic deviations and ensure the stability of movement. Figure 5.5 shows the changes in

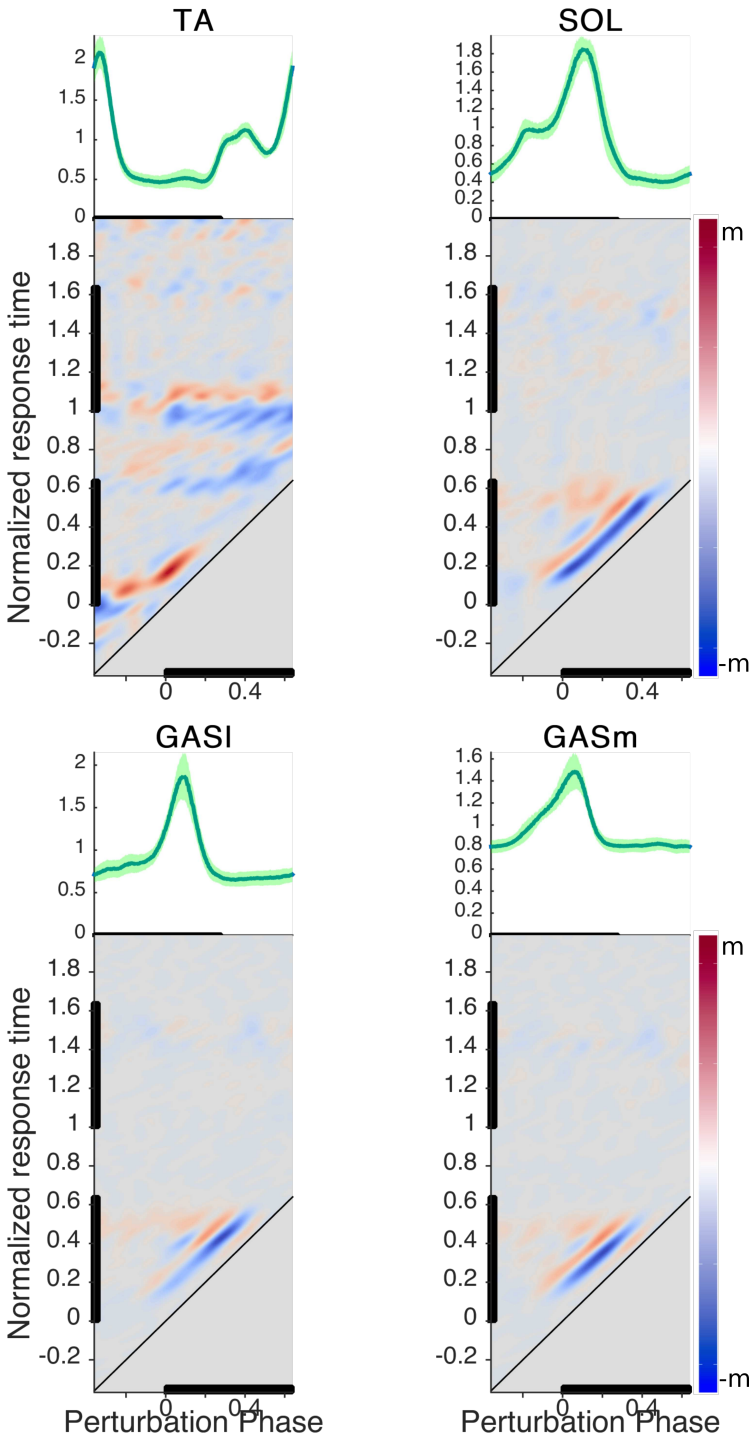

Figure 5.4. φIRFs for TA, SOL, GASl, and GASm during the first two cycles after onset of perturbations. The top plots in green show the mean waveforms. m = 16 mV.m^{-1}.

the lower leg EMG signals that succeed kinematic responses. Around the mid stance TA is inactive (Figure 5.5a) and the perturbation does not affect its level of activity (Figure 5.5b). At the same time, activation has started to increase in plantarflexors in preparation for push-off. The perturbation results in decreases in their activities with latencies of 80–120 msec. The contralateral muscles do not show any responses, which is not surprising given the lack of detectable responses in major contralateral kinematic variables discussed earlier.

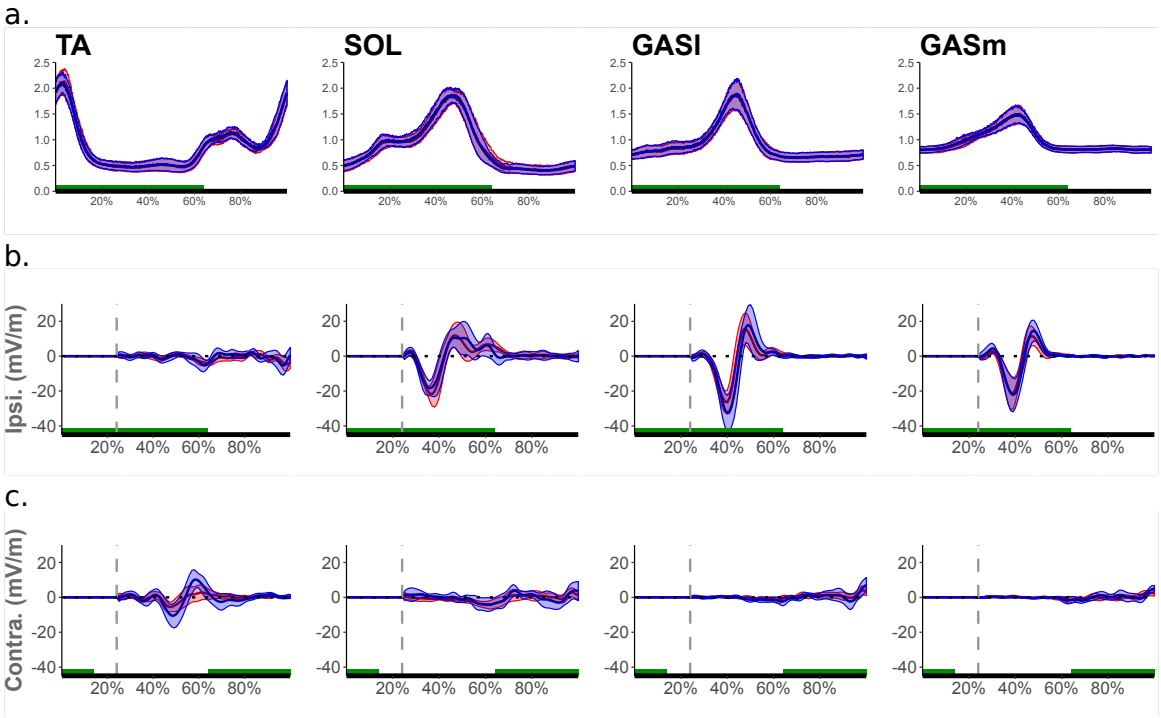

Figure 5.5. *EMG responses to single-support perturbation.* **a.** Mean waveforms of the EMGs from TA, SOL, GASl and GASm for the higher (red) and the lower (blue) perturbations. **b.** EMG responses of the ipsilateral leg. The grey dashed line marks the onset of perturbation and the green bar highlights the stance phase. **c.** EMG responses of the contralateral leg.

Figure 5.6 shows the transient changes in the upper leg muscles. Quadriceps are mainly active in early stance to straighten and stabilize the leg around the time

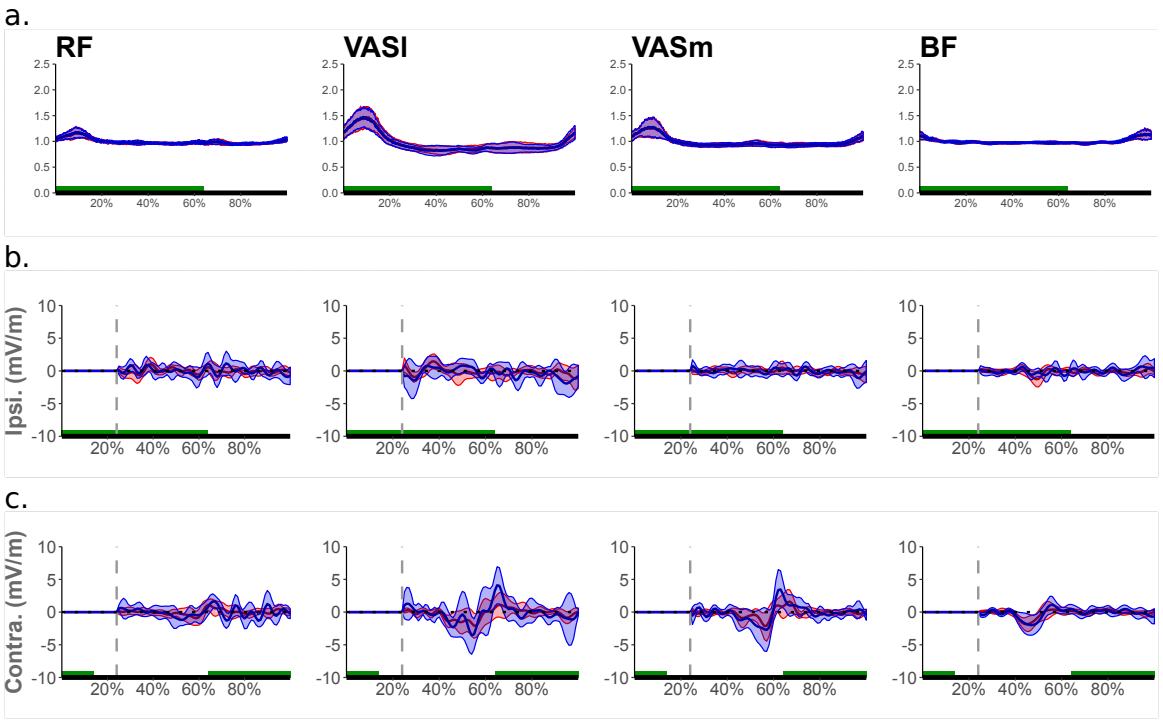

Figure 5.6. *EMG responses to single-support perturbation.* **a.** Mean waveforms of the EMGs from RF, VASl, VASm and BF for the higher (red) and the lower (blue) perturbations. **b.** EMG responses of the ipsilateral leg. The grey dashed line marks the onset of perturbation and the green bar highlights the stance phase. **c.** EMG responses of the contralateral leg.

of heel-strike (Figure 5.6a). During mid stance when ipsilateral quadriceps are quiet the perturbation does not result in significant responses (Figure 5.6b). The same is true for the contralateral quadriceps which are in the early swing (Figure 5.6c). BF is mainly active during the late swing and early stance neither of which coincide with the perturbations delivered around the mid stance. None of the legs show any responses in BF.

Kinematic responses to double-support perturbation. Another important phase of gait is the double-support phase. This is the only phase in which both legs can directly receive the effects of treadmill perturbations. As a result, we expect to see

some responses in the contralateral leg. Here the contralateral leg is the leg which is in late stance at the onset of perturbation while the ipsilateral leg is in early stance.

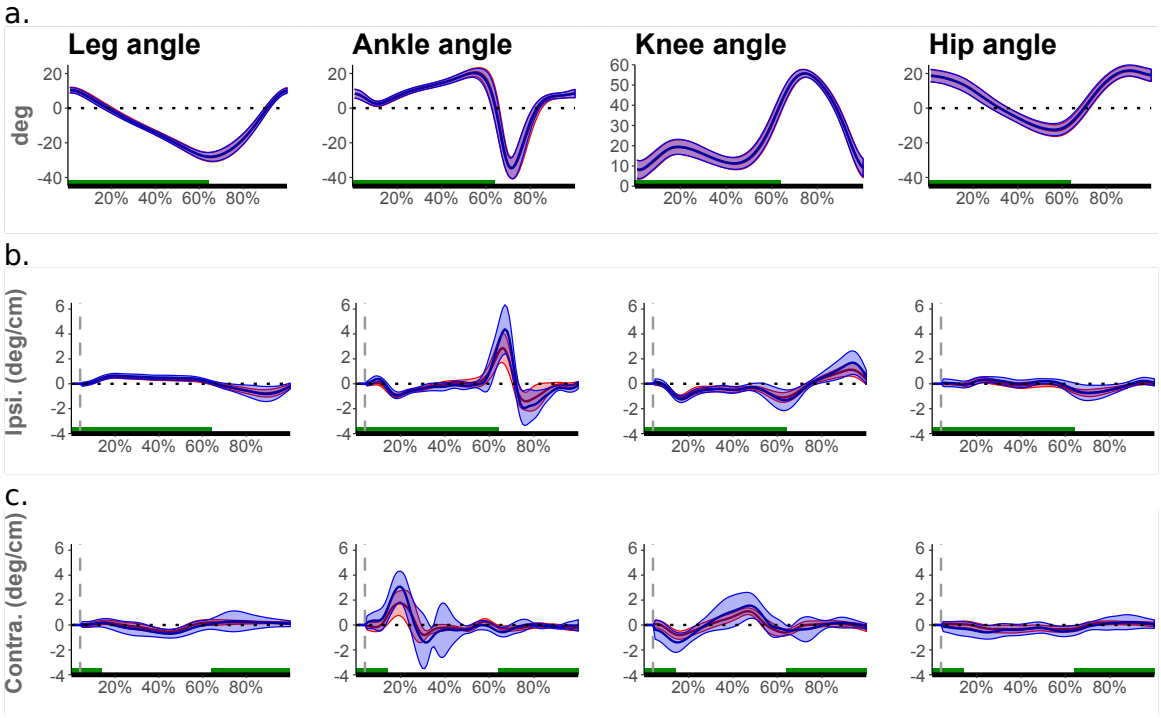

Figure 5.7. *Kinematic responses to double-support perturbation.* **a.** Mean waveforms for the leg angle and the ankle, knee and hip joint angles for the higher (red) and the lower (blue) perturbations. **b.** Kinematic responses of the ipsilateral leg. The grey dashed line marks the onset of perturbation and the green bar highlights the stance phase. **c.** Kinematic responses of the contralateral leg.

Figure 5.7 shows kinematic responses in the leg angle and joint angles. The perturbation is delivered at 4% of the cycle when the ipsilateral leg is in early stance and the contralateral leg is close to toe-off. The perturbation causes the leg to move forward (angle increase) and results in decreases in the ankle and knee angles similar to the effects of perturbation during single-support phase. However, unlike the single-support response, the ankle angle shows an apparent latency ($\sim$ 100 msec) to register any significant changes. This lack of significance can be attributed to the

large between-subject variability in the estimated responses close to the heel-strike. The contralateral leg shows an increase (dorsiflextion) in the ankle angle right after the onset. Close to the push-off, the contralateral heel has left the belt and the foot front is the only point of contact. Unlike the case for the single-support, at this configuration, a forward impulse in the treadmill belt results in a dorsiflexion.

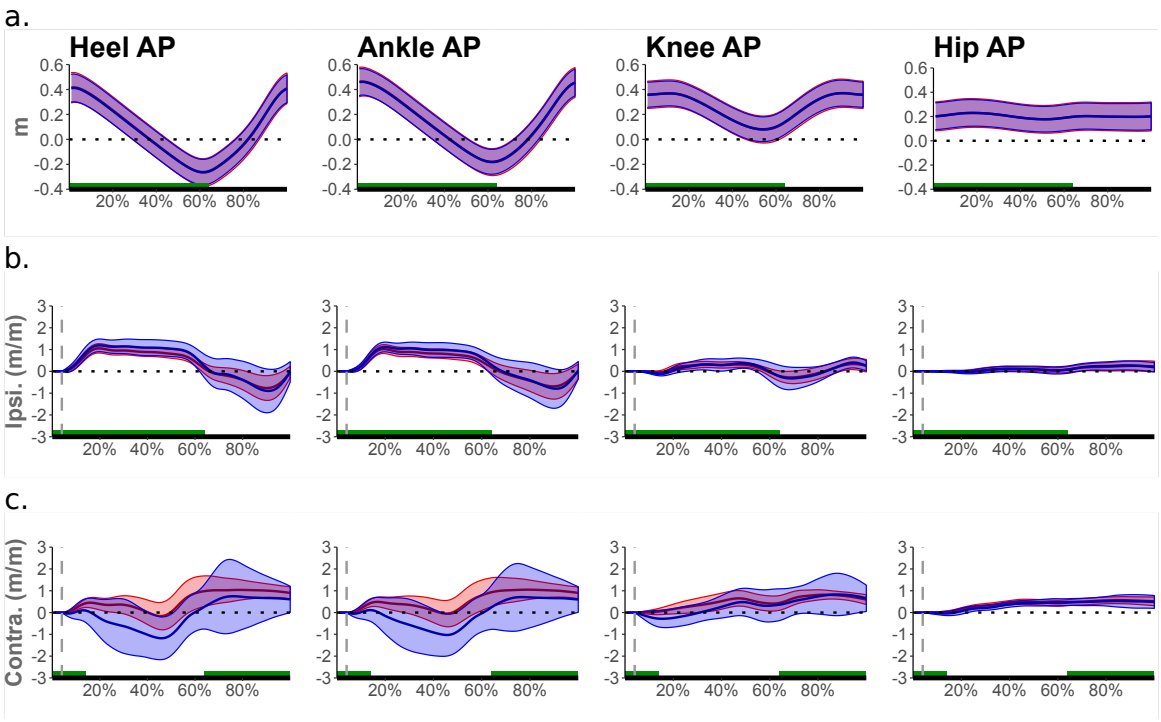

Figure 5.8. *Kinematic responses to double-support perturbation.* **a.** Mean waveforms for the heel, ankle, knee and hip markers AP trajectories for the higher (red) and the lower (blue) perturbations. **b.** Kinematic responses of the ipsilateral leg. The grey dashed line marks the onset of perturbation and the green bar highlights the stance phase. **c.** Kinematic responses of the contralateral leg.

The effects of perturbations on the kinematics of markers are depicted in Figure 5.8. Similar to the single-support responses the heel and ankle AP trajectories follow a step function during the stance mainly after heel-strike and before heel-off. The effect of perturbation on the AP movement of the knee is negligible. While the

ipsilateral hip does not show any significant response, the contralateral hip shows a small increase in the AP movement.

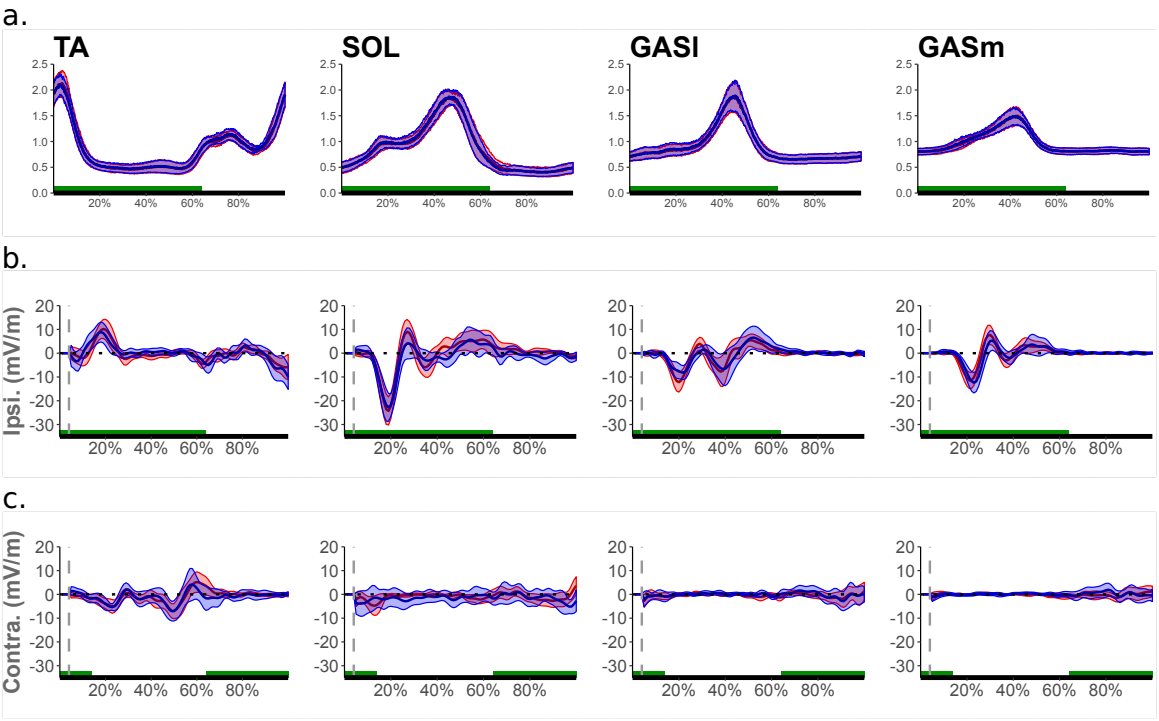

Figure 5.9. *EMG responses to double-support perturbation.* **a.** Mean waveforms of the EMGs from TA, SOL, GASl and GASm for the higher (red) and the lower (blue) perturbations. **b.** EMG responses of the ipsilateral leg. The grey dashed line marks the onset of perturbation and the green bar highlights the stance phase. **c.** EMG responses of the contralateral leg.

EMG responses to double-support perturbation. Figure 5.9 shows EMG responses of lower leg muscles during double-support. The perturbation elicits an increase in the activity of TA. This is in contrast to the single-support phase in which TA showed no responses. This can be attributed to the timing of perturbation. Close to the heel-strike TA is normally active (Figure 5.9a). So a modulation of its activity during this time is more plausible compared to when the muscle is quiet (e.g., mid stance). Plantarflexors show decreases in their activities. While

around the heel-strike the foot is not fully in touch with the belt and a positive impulse in the velocity may not create a large plantarflexion, the leg moves forward with a knee extension that straightens the leg and eliminates an urgent need for the gradual increase in the activity of plantarflexors observed in normal walking. In the contralateral leg, no responses are observed in the plantarflexors while TA shows a small decrease in its activity 130–170 msec after the onset. This can be attributed to the effect of perturbation which creates a dorsiflexion in the contralateral foot before push-off.

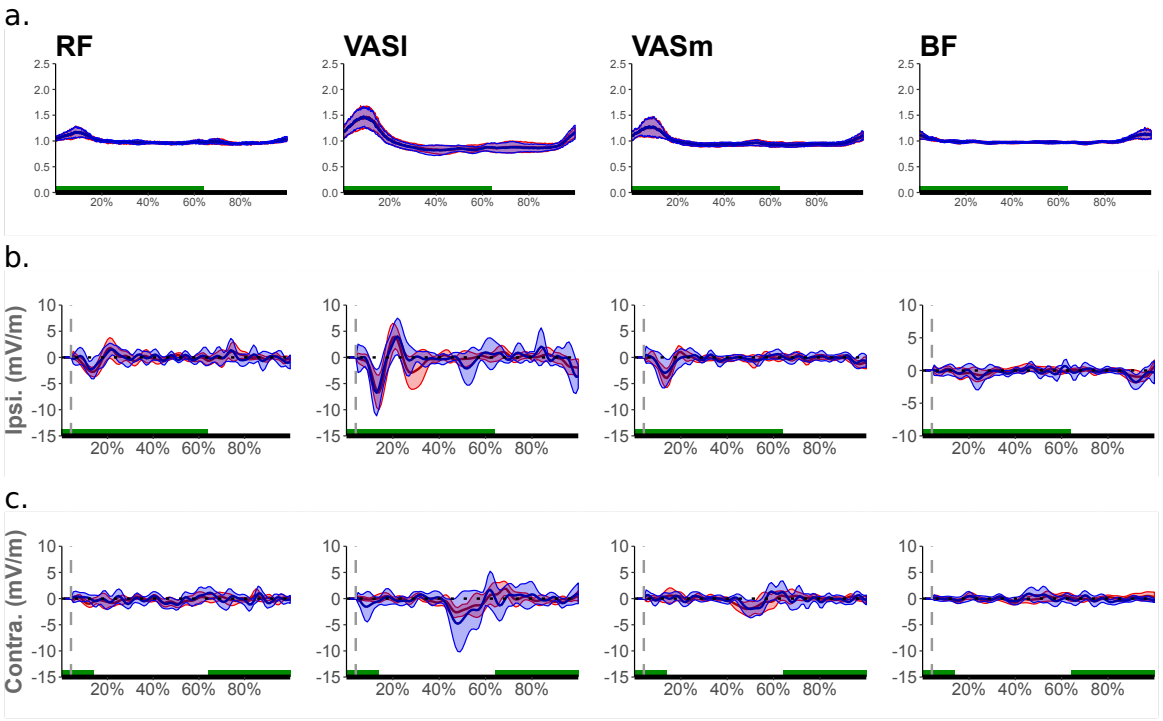

Figure 5.10. *EMG responses to single-support perturbation.* **a.** Mean waveforms of the EMGs from RF, VASl, VASm and BF for the higher (red) and the lower (blue) perturbations. **b.** EMG responses of the ipsilateral leg. The grey dashed line marks the onset of perturbation and the green bar highlights the stance phase. **c.** EMG responses of the contralateral leg.

The responses in the upper leg muscles are shown in Figure 5.10. Quadri-

ceps show decreases in their activities in response to perturbation. As mentioned before during early stance increases in the activities of plantarflexors and quadriceps together straightens the leg in preparation for COM to rise. Since the positive perturbation (i.e., deceleration) has already straightened the leg the activities of quadriceps decrease in concert with changes in plantarflexors. BF, on the other hand, does not show any significant response. The same is true for the upper leg muscles of the contralateral leg.

5.4 Discussion

Revisiting the goals of this study from the introduction section, here we showed that our computational approach successfully quantified responses to continuous mechanical perturbations of the treadmill. We observed responses in kinematics immediately after the onset of perturbations. To correct these immediate kinematic deviations, after some delay the nervous system modulates muscle activations. We observed significant responses in lower and upper leg muscles. These responses had latencies of 80–150 msec. Although with these values we cannot differentiate between medium and long latency responses [64], our approach provided a more realistic estimation of responses compared to a recent study [100] that used treadmill perturbations and reported latencies at 160–190 msec. Another major finding of our study was the observation of responses in TA. Many studies in the past have reported a lack of response from TA to mechanical perturbations [63, 64, 71, 100]. We showed that perturbations delivered close to the heel-strike, the phase at which

TA is normally active, result in responses from TA in concert with plantarflexor responses in an effort to stabilize gait.

With the application of small perturbations, the local limit cycle (LLC) approximation assumes that an increase of two fold in the input should result in the same increase in the output. Therefore the φIRF, which describes output amplitude divided by input amplitude, should not change. Using perturbations of two different amplitudes we tested this assumption. While the responses are not equal for both perturbations, in most cases the responses are very close. Thus the LLC approximation turned out to be reasonable. (However, see 5.4.1 below for a different perspective.)

Another goal of this study was to compare and contrast responses to mechanical perturbations to those observed from visual perturbations in previous chapters. Similar to visual responses, we saw mechanical responses for each muscle during the phases of the cycle in which the muscle was normally active. Although most kinematic variables and EMGs showed significant responses, some did not show any. This can be attributed to the possibility that mechanical perturbations created local disturbances which could be rejected using only a subset of muscles. Another difference was lack of any unexpected change in the activity of plantarflexors during mid stance. As it was shown in the experiments with visual perturbations, a perturbation that elicits responses to increase the walking speed registers significant transient decreases in plantarflexor activities at mid-stance before their activities increase during push-off (i.e., the expected behavior). We did not see such patterns of activity in mechanical responses. However, it is possible that the mechanical per-

turbation applied was not large enough to create substantial changes in the walking speed.

5.4.1 Limitations and future work

An important part of analyzing responses to mechanical perturbations is the estimation of latencies of reflexes. It is based on these latencies that reflexes and their origins can be categorized. Because of limitations in the input frequency bandwidth used here, our estimation of latencies may not be very accurate. However, the focus of our study was on identification of qualitative patterns of changes in the activity rather than estimation of reflex latencies. Regardless of this, the estimated responses showed latencies within ranges reported in the literature.

We measured EMG signals from only one leg and used the assumption of spatio-temporal symmetry to estimate responses of the contralateral leg. The assumption of symmetry has not been evaluated in the context of crossed reflexes before. Future studies can measure from both legs to assess the assumption of symmetry.

Our approach in this study assumed responses were equal in magnitude and opposite in sign for a change in direction of the perturbation. Some studies in the past [62,65,89] have reported significant differences in responses with a change in the direction of perturbation. However, the perturbations used in these studies might have been large enough that have caused nonlinear effects. We have used small perturbations in our experiment that allows us to assume a LLC approximation.

Future studies can further investigate any possible effect of changes in direction of the perturbation on transient responses.

This study quantified responses to mechanical perturbations of the treadmill. As discussed earlier in this chapter, these perturbations cannot independently probe all degrees of freedom involved in the control of walking. However, the application of perturbations to different degrees of freedom can provide information on responses and the strategies used to correct for kinematic deviations. Other studies have applied mechanical perturbations to the trunk and the foot during swing [126, 127]. Future studies can expand these efforts to other joints and degrees of freedom.

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